

LONDON  
SCHOOL of  
HYGIENE  
& TROPICAL  
MEDICINE



LSHTM Research Online

Chan, Xuanhao; (2015) Life course effects of anthropometric change among Singapore youth from 1990 to 2011. PhD thesis, London School of Hygiene & Tropical Medicine. DOI: <https://doi.org/10.17037/PUBS.02101871>

Downloaded from: <https://researchonline.lshtm.ac.uk/id/eprint/2101871/>

DOI: <https://doi.org/10.17037/PUBS.02101871>

**Usage Guidelines:**

Please refer to usage guidelines at <https://researchonline.lshtm.ac.uk/policies.html> or alternatively contact [researchonline@lshtm.ac.uk](mailto:researchonline@lshtm.ac.uk).

Available under license. To note, 3rd party material is not necessarily covered under this license: <http://creativecommons.org/licenses/by-nc-nd/3.0/>

<https://researchonline.lshtm.ac.uk>

LONDON  
SCHOOL *of*  
HYGIENE  
& TROPICAL  
MEDICINE



Life course effects of anthropometric change among Singapore youth  
from 1990 to 2011

XUANHAO CHAN

Thesis submitted in accordance with the requirements for the  
degree of  
Doctor of Philosophy  
University of London

January 2015

Department of Social and Environmental Health Research

Faculty of Public Health

LONDON SCHOOL OF HYGIENE & TROPICAL MEDICINE

Funded by Singapore Health Promotion Board

Research group affiliation(s): None

*I, Xuanhao Chan, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.*

## **Abstract**

### **Introduction**

The obesity epidemic is leading to wide-ranging public health problems and potentially reduced life expectancy. This thesis aims to characterise secular trends of anthropometric change among Singaporeans aged 6 to 18 and explore relationships of their latent body mass index (BMI) Z-score growth trajectories during childhood and adolescence on mental health status in later life. It also presents a systematic review of the evidence on the associations of weight change on later life health outcomes.

### **Methods**

The uniqueness of this research lies in the development of a new Singapore Longitudinal and Life Course Cohort (SLLCC), an extensive individual-level dataset of repeatedly measured anthropometric data, from about 2.7 million students born between 1973 to 2003, collected through routine annual school-based health screening programmes from 1990 to 2011. Life course growth models were used to model latent developmental trajectories in the SLLCC and age-period-cohort (APC) analyses were conducted to determine secular trends in BMI.

## **Results**

Cohorts of people born from 2000 to 2010 had successively higher body weights than cohorts born two decades earlier. These effects were attenuated when cohort influences were removed. Findings from piecewise linear regression and the Zivot-Andrews Unit Root test suggested an upward shift in obesity rates for children aged 6 to 12 years and a levelling off between ages 13 to 18, occurring around the year 2008.

In a sub-sample of 519 members of the SLLCC cohort linked with the 2010 National Health Survey, results from latent class growth mixture modelling suggested that individuals who experienced a distinct developmental trajectory of an increasing rate of weight gain from age 10 resulting in obesity at age 16 was associated with a 37% increased risk of later poor mental health well-being, all else held constant. This is the first study to show that cumulative duration of obesity during childhood and adolescence is associated with significant risks of psychological distress later in life.

## **Discussion**

The findings from this thesis could lead to new evidence-informed public health imperatives for investments to monitor early childhood growth development so as to mitigate deleterious effects on health, social and economic outcomes in adulthood.



*“Everything that can be counted does not necessarily count; everything that counts cannot necessarily be counted”*

**Albert Einstein**

## Table of Contents

<b>Abstract</b>	<b>2</b>
<b>List of tables</b>	<b>9</b>
<b>List of figures</b>	<b>14</b>
<b>Acknowledgements</b>	<b>18</b>
<b>Abbreviations</b>	<b>20</b>
<b>Introduction to thesis</b>	<b>21</b>
<b>Chapter 1: Background</b>	<b>26</b>
<i>1.1 BMI and early life predictors</i>	26
<i>1.2 Tracking of childhood overweight into adulthood</i>	31
<i>1.3 Applicability of developmental trajectories to depict risk exposures</i>	34
<i>1.4 Rationale for research</i>	36
1.4.1 Obesity situation in Singapore	36
1.4.2 Effect of weight change on later life	38
1.4.3 Childhood and adolescence as critical periods	41
<i>1.5 Research aim and objectives</i>	43
<i>1.6 Data sources</i>	46
1.6.1 Health Promotion Board	46
1.6.2 Ministry of Education	48
1.6.3 Ministry of Health	48
<b>Chapter 2: Systematic review</b>	<b>49</b>
<i>2.1 Introduction</i>	49
<i>2.2 Search strategy</i>	51
<i>2.3 Data extraction process</i>	56
<i>2.4 Characteristics of Included Studies</i>	77
<i>2.5 Quality of evidence</i>	79
<i>2.6 Main findings</i>	81
2.6.1 All-cause mortality	81
2.6.2 CVS mortality	96
2.6.3 CHD mortality	103
2.6.4 First incidence of CHD	109
<i>2.7 Methodological issues</i>	113
2.7.1 Temporal separation	113
2.7.2 Studies with measurements at only two-time points	114
2.7.3 Weight fluctuation	114
2.7.4 Cox's proportional model	116
<i>2.8 Discussion</i>	117
<i>2.9 Conclusions</i>	122
<b>Chapter 3: Data sources and preparation</b>	<b>124</b>
<i>3.1 Introduction</i>	125
3.1.1 Brief history of Singapore's School Health Service	125
<i>3.2 Health Promotion Board</i>	127
3.2.1 Youth Health Division	127
3.2.2 Health screening in primary schools	128
3.2.3 Health screening in secondary schools	130

3.2.4 School-based immunisation	131
3.2.5 Computerised data management system	131
3.2.6 School Health Centre	132
3.3 <i>Ministry of Education</i>	133
3.3.1 Trim and Fit	133
3.3.2 Holistic Health Framework	135
3.4 <i>Ministry of Health</i>	136
3.4.1 National Health Survey 2010	136
3.5 <i>Ethics approval for this PhD research</i>	137
3.6 <i>Thesis data sources</i>	139
3.6.1 SHS dataset	139
3.6.2 TAF dataset	140
3.6.3 NHS2010 dataset	141
3.7 <i>Data preparation</i>	141
3.7.1 General procedures	141
3.7.2 Data merge	145
3.7.3 Timeline	151
3.8 <i>Conclusion</i>	153
<b>Chapter 4: Cohort profile of the Singapore Longitudinal and Life Course Cohort (SLLCC)</b>	<b>154</b>
4.1 <i>Background</i>	155
4.1.1 Context	155
4.1.2 Summary of Singapore Cohorts	156
4.2 <i>SLLCC cohort profile</i>	161
4.2.1 Why was this new cohort established?	161
4.2.2 Who is in the cohort?	164
4.2.3 Which variables are available?	166
4.2.4 Data preparation	171
4.3 <i>Characteristics of cohort</i>	172
4.4 <i>What are the strengths and weakness of the SLLCC?</i>	175
4.5 <i>Accessibility of the data</i>	177
4.6 <i>Conclusions</i>	177
<b>Chapter 5: Anthropometric change over time in Singapore youth from 1990 to 2011</b>	<b>180</b>
5.1 <i>Introduction</i>	181
5.2 <i>The obesity plateau phenomena</i>	184
5.3 <i>Singapore anthropometric studies</i>	185
5.4 <i>Classification of obesity and overweight</i>	187
5.2 <i>Aim of this new study</i>	189
5.3 <i>Methods</i>	190
5.3.1 Data sets	190
5.3.2 Investigation of possible levelling of obesity trends	192
5.3.3 Age, period, cohort effects	192
5.3.4 Difference in classification of obesity	194
5.4 <i>Results</i>	194
5.4.1 Possible levelling of obesity situation	194
5.4.2 Age, period, cohort effects	197
5.4.3 Difference in classification of obesity	210
5.5 <i>Discussion</i>	212
5.5.1 Is there a possible levelling of the obesity situation in Singapore and do trends differ for boys and girls?	212

5.5.2 What are the age, period and cohort effects influencing obesity trends among school-age children in Singapore?	214
5.5.3 Is there a difference in estimating the extent of the obesity situation in school-age children in Singapore from 1997 to 2011 using international BMI age- and gender-specific cut offs based on WHO Child Growth Standards versus the existing practice of using nutritional status?	217
5.6 <i>Strengths and limitations of this analysis</i>	219
5.7 <i>Conclusion</i>	221
<b>Chapter 6: Latent growth trajectories of body mass index in Singapore adolescents from 1990 to 2011</b>	<b>223</b>
6.1 <i>Introduction</i>	224
6.2 <i>Methods</i>	229
6.2.1 Data sets	229
6.2.2 Variables	230
6.2.3 Data preparation	231
6.2.4 Statistical analysis methods	231
6.3 <i>Results</i>	236
6.3.1 General analysis	236
6.3.2 Latent class analysis	239
6.3.3 Growth Mixture Models	241
6.3.4 Missing data	253
6.4 <i>Discussion</i>	254
6.5 <i>Strengths and limitations</i>	263
6.6 <i>Conclusions</i>	265
<b>Chapter 7: Understanding relationships between childhood and adolescence developmental trajectories with mental health well being in Singapore</b>	<b>267</b>
7.1 <i>Introduction</i>	268
7.2 <i>Aim of the study</i>	276
7.3 <i>Methods</i>	276
7.3.1 Study cohort	276
7.3.2 Mental health measurement	278
7.3.3 Growth trajectory variable	280
7.3.4 Covariates	281
7.3.5 Statistical analysis	283
7.4 <i>Results</i>	285
7.5 <i>Discussion</i>	298
7.6 <i>Conclusion</i>	307
<b>Chapter 8: Summary of findings and discussion</b>	<b>308</b>
8.1 <i>Introduction</i>	308
8.2 <i>Singapore context</i>	308
8.3 <i>Summary of the main datasets used in this thesis</i>	309
8.4 <i>Summary of key novel findings</i>	311
8.4.1 Effect of weight change on later life health outcomes	311
8.4.2 Secular trends of childhood obesity	311
8.4.3 Possible levelling of obesity trends	313
8.4.4 Latent growth trajectories	313
8.4.5 Growth trajectories and mental health	316
8.5 <i>Discussion</i>	318
8.5.1 Effect of weight change on later life health outcomes	318

8.5.2 Secular trends of childhood obesity	319
8.5.3 Possible levelling of obesity trends	322
8.5.4 Latent growth trajectories	329
8.5.5 Growth trajectories and mental health	332
8.6 <i>Areas for future work</i>	334
8.7 <i>Further extension of the SLLCC</i>	337
8.8 <i>Conclusions</i>	339
<b>References</b>	<b>341</b>

## List of tables

Table 1 Characteristics of the studies (n=30) included in the systematic review on association of weight change with all-cause and cause-specific mortality (CVS/CHD).....	58
Table 2 Methods of expressing weight or BMI change in the 30 studies included in the systematic review of association of weight change with all-cause and cause-specific mortality .	64
Table 3 Quality assessment of evidence of the 30 studies included in the systematic review of the association of weight change with all-cause and cause-specific mortality using the EPHPP tool	72
Table 4 Number of confounding factors adjusted for in the 30 studies included in the systematic review of the association of weight change with all-cause and cause-specific mortality .....	74
Table 5 Forest plots comparing Included Studies that measured the difference in weight between two study examinations (study type 1) for the association between weight change with all-cause mortality .....	84
Table 6 Forest plots comparing Included Studies that measured the difference between current weight and one or more recalled weight in young adulthood (study type 2) for the association between weight change with all-cause mortality.....	85
Table 7 Forest plots comparing Included Studies that measured the trend of weight over a series of examinations (study type 4) with one or more recalled weight in young adulthood (study type 5) for the association between weight change with all-cause mortality .....	90
Table 8 Forest plots comparing Included Studies that measured weight cycling (study type 6) for the association between weight change with all-cause mortality .....	91
Table 9 Forest plots comparing Included Studies on the relative risks associated between subgroups of greatest weight gain versus reference group with all-cause mortality.....	92
Table 10 Forest plots comparing Included Studies on the relative risk associated between subgroups of greatest weight loss versus reference group with all-cause mortality .....	93
Table 11 Forest plots comparing Included Studies on the relative risk associated between subgroups of greatest weight fluctuation versus reference group with all-cause mortality .....	94
Table 12 Forest plots comparing Included Studies with Strong EPHPP evidence rating for the association between weight change with all-cause mortality.....	95
Table 13 Forest plots comparing Included Studies with different study design types for the association between weight change with CVS mortality .....	98
Table 14 Forest plots comparing Included Studies with Strong EPHPP evidence rating for the association between weight change with CVS mortality .....	99

Table 15 Forest plots comparing Included Studies on the relative risk association between subgroups of greatest weight gain versus reference group with CVS mortality .....	100
Table 16 Forest plots comparing Included Studies on the relative risk association between subgroups of greatest weight loss versus reference group with CVS mortality .....	101
Table 17 Forest plots comparing Included Studies on the relative risk association between subgroups of greatest weight fluctuation versus reference group with CVS mortality .....	102
Table 18 Forest plots comparing Included Studies with different study design types for the association between weight change with CHD mortality .....	105
Table 19 Forest plots comparing Included Studies with Strong EPHPP evidence rating for the association between weight change with CHD mortality .....	106
Table 20 Forest plots comparing Included Studies on the relative risk association between subgroups of greatest weight gain versus reference group with CHD mortality .....	107
Table 21 Forest plots comparing Included Studies on the relative risk association between subgroups of greatest weight loss versus reference group with CHD mortality .....	108
Table 22 Forest plots comparing Included Studies on the relative risk association between subgroups of greatest weight fluctuation versus reference groups with CHD mortality .....	108
Table 23 Forest plots comparing Included Studies with different study design types for the association between weight change with first incidence of CHD .....	110
Table 24 Forest plots comparing Included Studies with Strong EPHPP evidence rating for the association between weight change with first incidence of CHD .....	111
Table 25 Forest plots comparing Included Studies on the relative risk association between subgroups of greatest weight gain versus reference group with first incidence of CHD .....	111
Table 26 Forest plots comparing Included Studies on the relative risk association between subgroups of greatest weight loss versus reference group with first incidence of CHD .....	112
Table 27 Number of records and type of independent variables available in School Health Service, Trim and Fit (thesis data sources) and those included in Master Dataset A .....	143
Table 28 An example of how BMI data for an individual record is linked across ages by their unique identifier combining data from different data sources in Master Dataset A .....	144
Table 29 Number of records available per year in both School Health Service and Trim and Fit data sources .....	144

Table 30 Estimated age at each academic level in Singapore for females and males .....	146
Table 31 Categorical variable labels assigned to students belonging to different race groups ...	146
Table 32 Summary of selected longitudinal cohorts relevant to the study of obesity in Singapore .....	157
Table 33 WHO classification of body mass index (BMI) .....	167
Table 34 Race and gender distribution in the Singapore Longitudinal and Life Course Cohort (SLLCC) .....	173
Table 35 BMI Z-scores summary statistics of subjects in the Singapore Longitudinal and Life Course Cohort (SLLCC) .....	174
Table 36 Effective sample sizes based on the number of BMI Z-scores recorded from age 6 to 18 in the Singapore Longitudinal and Life Course Cohort (SLLCC) .....	175
Table 37 Piecewise linear regression of obesity trends in children aged 6 to 18 in Singapore from 1997 to 2011 (with change in trend detected in 2008) .....	197
Table 38 Demography and weight profile of school-age children in Singapore in 1997 .....	198
Table 39 Age-period contingency table for mean % obesity among children aged 6 to 18 in Singapore from 1997 to 2011 .....	207
Table 40 Birth cohort effect on obesity rates of children aged 6 to 18 in Singapore .....	208
Table 41 Percentage of girls in Singapore classified as "obese" using WHO Child Growth Standards as compared if classified using Nutrition Status cut-offs from 1997 to 2010 .....	211
Table 42 Percentage of boys in Singapore classified as "obese" using WHO Child Growth Standards as compared if classified using Nutrition Status cut-offs from 1997 to 2010 .....	211
Table 43 Gender and race profile of study sample of students with at least 5 BMI measurements as compared to total SLLCC cohort .....	230
Table 44 Summary statistics of study sample of SLLCC that has at least 5 BMI measurements from age 7 to 16 .....	237
Table 45 Mean BMI-for-age Z-score distribution by age, gender and race groups in the study sample of SLLCC that has at least 5 BMI measurements from age 7 to 16 .....	237
Table 46 Median BMI-for-age Z-score distribution by age, gender and race groups in the study sample of SLLCC that has at least 5 BMI measurements from age 7 to 16 .....	238



Table 47 Goodness of fit indices of 7 latent class growth models using study sample of SLLCC that has at least 5 BMI measurements from age 7 to 16.....	240
Table 48 Parameters in a piecewise quadratic growth model of BMI-for-age Z-scores using study sample of SLLCC that has at least 5 BMI measurements from age 7 to 16.....	241
Table 49 Class counts and proportions of estimated latent class growth mixture models using the study sample of SLLCC that has at least 5 BMI measurements from age 7 to 16 .....	242
Table 50 Summary results of the best fitted latent class growth mixture model of 4 BMI-for-age Z-score trajectory classes in the study sample of SLLCC that has at least 5 BMI measurements from age 7 to 16.....	244
Table 51 Average latent class probabilities for the most likely latent class membership (row) by latent class (column) in the best fitted 4-class latent class growth mixture model in the study sample of SLLCC that has at least 5 BMI measurements from age 7 to 16.....	249
Table 52 Characteristics of students in the 4-class trajectories of the best fitted latent class growth mixture model using study sample of SLLCC that has at least 5 BMI measurements from age 7 to 16 .....	252
Table 53 Missing values in study sample of SLLCC with at least 5 BMI measurements from age 7 to 16 .....	253
Table 54 Missing BMI Z-score values at each age in the best fitted 4-class latent class growth mixture model in the study sample of SLLCC that has at least 5 BMI measurements from age 7 to 16 .....	254
Table 55 Socio-demographic profiles of SLLCC/NHS2010 linked study sample, the National Health Survey 2010 and the Singapore resident population aged 18 to 79 in 2010.....	286
Table 56 Gender and race distribution in the SLLCC/NHS2010 linked study sample of 519 individuals .....	286
Table 57 Age-specific prevalence of poor mental health by gender in the National Health Survey 2010 .....	287
Table 58 Summary statistics for BMI Z-scores in SLLCC/NHS2010 linked study sample of 519 individuals .....	287
Table 59 Frequency of BMI measurements by gender in the linked SLLCC/NHS2010 study sample of 519 individuals.....	288

Table 60 Average latent class probabilities for the most likely class membership (row) by latent class (column) in the best fitted 3-class trajectories latent class growth mixture model of the SLLCC/NHS2010 linked study sample of 519 individuals .....	290
Table 61 Characteristics of the latent BMI Z-score trajectory groups in the best fitted 3-class trajectories model of the SLLCC/NHS2010 linked study sample of 519 individuals .....	290
Table 62 Model results of univariate logistic regression on dependent variable of mental health status (GHQ-12) with reference on "Consistently Underweight" BMI trajectory class and Chinese race in SLLCC/NHS2010 linked study sample of 519 individuals .....	295
Table 63 Predictive margins of childhood and adolescence latent BMI Z-score trajectory classes on mental health well being (GHQ-12 score) in the SLLCC/NHS2010 linked study sample of 519 individuals .....	296
Table 64 Number of years being obese ( $BMI > 30\text{kg/m}^2$ ) by gender in the SLLCC/NHS2010 linked study sample of 519 individuals .....	296
Table 65 Predictive margins of duration of obesity (number of years) on mental health well being (GHQ12 score $>3$ ) in the SLLCC/NHS2010 linked study sample of 519 individuals .....	297

## List of figures

Figure 1 PRISMA flowchart of the systematic review on the association of weight change on all-cause and cause-specific mortality .....	56
Figure 2 Timeline for development of study protocol, data request and preparation for the thesis (Feb 2012 to Aug 2013) .....	152
Figure 3 Age-period-cohort data structure of the Singapore Longitudinal and life Course Cohort (SLLCC) .....	172
Figure 4 Mean annual percentage obese among children ages 6 to 18 from 1997 to 2011 in Singapore .....	195
Figure 5 Differences in mean annual percentage obese between boys and girls aged 6 to 18 from 1997 to 2011 in Singapore .....	195
Figure 6 Obesity trends in boys and girls aged 6 to 12 in Singapore from 1997 to 2011 .....	196
Figure 7 Obesity trends in boys and girls aged 13 to 18 in Singapore from 1997 to 2011 .....	196
Figure 8 Age-period obesity ( $\text{BMI} > 30\text{kg/m}^2$ ) trends among children aged 6 to 18 in Singapore from 1997 to 2011 .....	200
Figure 9 Age-period overweight ( $\text{BMI} 25 \text{ to } 30\text{kg/m}^2$ ) trends among children aged 6 to 18 in Singapore from 1997 to 2011 .....	200
Figure 10 Age-period grade 1 thinness ( $\text{BMI} 17 \text{ to } 18.5\text{kg/m}^2$ ) trends among children aged 6 to 18 in Singapore from 1997 to 2011 .....	201
Figure 11 Age-period grade 2 thinness ( $\text{BMI} 16 \text{ to } 17\text{kg/m}^2$ ) trends among children aged 6 to 18 in Singapore from 1997 to 2011 .....	201
Figure 12 Age-period grade 3 thinness ( $\text{BMI} < 16\text{kg/m}^2$ ) trends among children aged 6 to 18 in Singapore from 1997 to 2011 .....	202
Figure 13 Annual obesity trends ( $\text{BMI} > 30\text{kg/m}^2$ ) among children aged 6 to 18 by race groups in Singapore from 1997 to 2011 .....	202
Figure 14 Percentage obesity ( $\text{BMI} > 30\text{kg/m}^2$ ) of each race groups at ages 6 to 18 in Singapore from 1997 to 2011 .....	203
Figure 15 Age-cohort obese ( $\text{BMI} > 30\text{kg/m}^2$ ) trends among children aged 6 to 18 born from 1983 to 2003 in Singapore .....	204
Figure 16 Age-cohort overweight ( $\text{BMI} 25 \text{ to } 30\text{kg/m}^2$ ) trends among children aged 6 to 18 born from 1983 to 2003 in Singapore .....	204

Figure 17 Age-cohort grade 1 Thinness (BMI 17 to 18.5kg/m <sup>2</sup> ) trends among children aged 6 to 18 born from 1983 to 2003 in Singapore.....	205
Figure 18 Age-cohort grade 2 Thinness (BMI 16 to 17kg/m <sup>2</sup> ) trends among children aged 6 to 18 born from 1983 to 2003 in Singapore.....	205
Figure 19 Age-cohort grade 3 Thinness (BMI < 16kg/m <sup>2</sup> ) trends among children aged 6 to 18 born from 1983 to 2003 in Singapore.....	206
Figure 20 Residual means from median polish by birth cohort of children aged 6 to 18 in Singapore .....	209
Figure 21 Age-period obesity trends of children born in 1980, 1985, 1990, 1995 and 2000 with and without cohort effects .....	209
Figure 22 Directed acyclic graph of the association between life course social economic position and later life health, adapted from (250) .....	225
Figure 23 Example of linear latent class growth model with continuous BMI-for-age Z-score, SLLCC, 1990 to 2011 .....	232
Figure 24 Example of piecewise linear latent class growth model with continuous BMI-for-age Z-score, SLLCC, 1990-2011 .....	233
Figure 25 Example of linear latent class growth model with two parallel processes for continuous BMI-for-age Z-score with regression among random effects, SLLCC, 1990-2011 .....	234
Figure 26 Mean BMI-for-age Z-score by gender in the study sample of SLLCC that has at least 5 BMI measurements from age 7 to 16 .....	238
Figure 27 BMI-for-age Z-score distribution by race groups in the study sample of SLLCC that has at least 5 BMI measurements from age 7 to 16.....	239
Figure 28 Plot of BIC values versus number of class in a latent class growth mixture model of BMI-for-age Z-scores in the study sample of SLLCC that has at least 5 BMI measurements from age 7 to 16 .....	242
Figure 29 Best fitted latent class growth mixture model of 4 BMI-for-age Z-score trajectory classes in the study sample of SLLCC that has at least 5 BMI measurements from age 7 to 16	243
Figure 30 Random subset of students in the "Pubertal-Only Overweight" trajectory group (class 1) in the best fitted 4-class latent class growth mixture model in the study sample of SLLCC that has at least 5 BMI measurements from age 7 to 16.....	244
Figure 31 Pubertal-Only Overweight trajectory group: within-class BMI weight classification prevalence.....	245

Figure 32 Random subset of students in the "Normal-Underweight" trajectory group (class 2) in the best fitted 4-class latent class growth mixture model in the study sample of SLLCC that has at least 5 BMI measurements from age 7 to 16 .....	246
Figure 33 Normal-Underweight trajectory group: within-class BMI weight classification prevalence .....	246
Figure 34 Random subset of students in the "Consistently Obese" trajectory group (class 3) in the best fitted 4-class latent class growth mixture model in the study sample of SLLCC that has at least 5 BMI measurements from age 7 to 16 .....	247
Figure 35 Consistently Obese trajectory group: within-class BMI weight classification prevalence .....	247
Figure 36 Random subset of students in the "Consistently Underweight" trajectory group (class 4) in the best fitted 4-class latent class growth mixture model in the study sample of SLLCC that has at least 5 BMI measurements from age 7 to 16 .....	248
Figure 37 Consistently Underweight trajectory group: within-class BMI weight classification prevalence .....	248
Figure 38 Gender differences in the best fitted 4-class latent class growth mixture model in the study sample of SLLCC that has at least 5 BMI measurements from age 7 to 16 .....	250
Figure 39 Mean BMI Z-scores of boys and girls in the Pubertal-Only Overweight trajectory group of the study sample of SLLCC that has at least 5 BMI measurements from age 7 to 16 .....	250
Figure 40 Mean BMI Z-scores of boys and girls in the Normal-Underweight trajectory group of the study sample of SLLCC that has at least 5 BMI measurements from age 7 to 16 .....	251
Figure 41 Mean BMI Z-scores of boys and girls in the Consistently Obese trajectory group of the study sample of SLLCC that has at least 5 BMI measurements from age 7 to 16 .....	251
Figure 42 Mean BMI Z-scores of boys and girls in the Consistently Underweight trajectory group of the study sample of SLLCC that has at least 5 BMI measurements from age 7 to 16 .....	252
Figure 43 Indicators of model fit (BIC values) in the latent class growth mixture models of the SLLCC/NHS2010 linked study sample of 519 individuals .....	289
Figure 44 Latent BMI Z-score trajectory groups in the best fitted 3-class trajectories model of the SLLCC/NHS2010 linked study sample of 519 individuals .....	289
Figure 45 Random subset of students in the "Consistently Underweight" trajectory group (class 1) in the best fitted 3-class latent class growth mixture model in the SLLCC/NHS2010 linked study sample of 519 individuals .....	291

Figure 46 Random subset of students in the "Consistently Overweight" trajectory group (class 2) in the best fitted 3-class latent class growth mixture model in the SLLCC/NHS2010 linked study sample of 519 individuals.....292

Figure 47 Random subset of students in the "Adolescence-Onset Obesity" trajectory group (class 3) in the best fitted 3-class latent class growth mixture model in the SLLCC/NHS2010 linked study sample of 519 individuals .....292

Figure 48 Predictive margins of latent BMI Z-score trajectory class and duration of obesity on probability of poor mental health status (GHQ-12 score >3) in the SLLCC/NHS2010 study sample of 519 individuals.....297

## Acknowledgements

I would like to first express my gratitude to Dr Vijaya K, Dr Foo Ling Li, Dr Chan Mei Fen, Dr Veronica Tay, Ms Aslyn Koh and Ms Jeanette Lau at the Health Promotion Board of Singapore for supporting my PhD. I am also indebted to Ms Connie Yeo, Mr Goh Tong Wee, Ms Soh Mei Ling and Mr Toh Chee Keong at the Ministry of Education and Dr Stefan Ma, Dr Derrick Heng and Mr Fong Chee Weng at the Ministry of Health as collaborators for the research.

About four years ago, for some reason, I chose to pursue a so-called “PhD” or more commonly famed as “Permanent Head Damage” among those who dare desire to attain the highest academic accolade. Here I am, at the end of this journey, to share a glimpse of my undertaking with a new unknown friend, you, the Reader. This personal piece of work is dedicated to all those who re-read this section after going through all 368 pages.

Research to me is analogous to embarking on a long trek to scale the greatest peaks of the world. One would typically start off with a light heart, celebrating life as it is but in reality, there are going to be numerous times when you would constantly question why you would choose to pay for the experience only to suffer in pain, 90% of the time. And when you reach the Summit, the view might actually be not that spectacular and before you, lays the equally arduous descent. Despite encountering many challenges along the way, I have now completed my expedition and I am sincerely glad to have two of the best trekking guides, Professor Mark Petticrew and Dr Kiran Nanchahal, who were both extremely understanding and patient with me in the past four years. I really appreciate your attention to details and always providing constructive guidance on

my work. Also, thanks to Dr Richard Silverwood, Professor Bianca de Stavola and Professor Truls Ostbye for being on my Advisory Committee.

All of these would not have been possible without the emotional support of my wife, Pauline, who believed in our future and me. To my Parents: “I did it” and “yes, I have saved at least three backups of my thesis in all different locations”.

Completing this PhD dissertation marks a major achievement in my life and as the saying goes “all good things must come to an end, so that better things can follow”. Finally, I would like to thank everyone who has contributed to my work and life in one way or another.



## Abbreviations

APC	Age-Period-Cohort
BMI	Body Mass Index
CHD	Coronary Heart Disease
CVS	Cardiovascular
HPB	Health Promotion Board
LCA	Latent Class Analysis
LCGMM	Latent Class Growth Mixture Modelling
MOE	Ministry of Education
MOH	Ministry of Health
NHS	National Health Survey
NRIC	National Registration Identification Card
RR	Relative Risk
SEP	Socio-Economic Position
SHS	School Health Service
SLLCC	Singapore Longitudinal and Life Course Cohort
TAF	Trim and Fit

## Introduction to thesis

The obesity epidemic is currently tending to lead to wide-ranging public health problems and even reduce life expectancy (1-3) although an emerging set of studies on adolescents in western populations has shown that the prevalence of obesity might have reached a plateau in the recent years in some countries (4-6). The global concern about the ill-effects of obesity, as defined by a high body mass index greater than  $30\text{kg/m}^2$ , has largely been guided by several large systematic reviews that have consistently reported a positive dose-response association of early life BMI with all-cause mortality and other cause-specific mortality later in life (2, 7). The majority of studies associating early development with later disease have used birth weight as an index of foetal growth, with low birth weight being shown to be predictive of increased subsequent disease risk (8-10). However, such approaches have been shown to be flawed as when associations of weight at birth with a later adverse outcome becomes strengthened when adjusted for adult size, it is the change in size across the whole time interval between the measurements, not just in early life, that is implicated (11).

In relation to the literature on weight change, several other studies have also focused on the contribution to risk of weight fluctuation, where in both western and Asian populations, observations include a linear trend of increasing weight variability associated with increasing risk of all-cause mortality in sub-groups of individuals with high weight fluctuation versus a stable weight reference group (12-18). Intentional or purposeful weight loss and subsequent weight gain are difficult to disentangle as such weight cycling patterns may have different causes and effects in obese and non-obese individuals. However study designs used to define and

evaluate weight cycling vary markedly (19) and findings from limited large-scale studies are still insufficient to alter public health recommendations regarding weight control (20).

Scientifically, these findings may be helpful for epidemiologists but for the public health programme manager, it raises several questions: should we be continuing our focus on getting people to lose weight or asking them to maintain their current weight? How about the long-term effects of weight changes during childhood and adolescence? The phenomenon of weight fluctuation is particularly pertinent in a modern society, as in Singapore, where periods of dieting and binge eating can easily lead to weight fluctuations over short periods of time. One aspect seems clear: the increased relative risks associated with large changes in weight, both gains and losses, at least among adults, should be considered in future weight management or obesity prevention programmes. Until now, there have been few studies exploring the aetiology of obesity among children and adolescents in Singapore.

Therefore, the overall aim of this thesis is to characterise anthropometric change among Singapore youth from 1990 to 2011 and explore relationships of their latent growth trajectories during childhood and adolescence on later health outcomes.

The introductory Chapter One provides an overview of the obesity situation globally and in Singapore with an objective to outline the rationale for my research questions. Chapter Two is a systematic review of the evidence on the associations of weight change on later life health outcomes, which also served to identify methods used to characterise anthropometric change and evaluate the types of existing longitudinal studies related to studying obesity around the world.

Chapter Three describes details of data preparation in order to establish a new Singapore Longitudinal and Life Course Cohort (SLLCC) for the purposes of this thesis. The full epidemiological cohort profile of the SLLCC is then presented in Chapter Four.

The epidemiological transition leading to higher prevalence of non-communicable diseases associated with overweight and obesity is evident from the increasing trends observed in prevalence of Type II diabetes and hypercholesterolemia in Singapore (21). These shifts were largely associated with behavioural changes in dietary profile and lifestyle and decreased levels of physical activity (21). The SLLCC is the largest and only longitudinal cohort of school-age children from age 7 to 16 who were born from 1973 to 2003 in Singapore. Chapter Five explores secular trends through age, period and cohort (APC) analytical approaches to evaluate their impact on obesity trends among school-age children in Singapore in the last two decades. In that chapter, I will also explore the possible levelling of the obesity situation in Singapore and whether these trends differ for boys and girls.

One general shortcoming of previous research in this field is that quantification of the association of BMI as a risk factor for mortality has been principally based on severity or extent of overweight at a single point in time. Recent studies have invoked a shift from undue emphasis on the consequences of low birth weight to a broader appreciation of the long-term effects of growth throughout the developmental period and across the entire range of body size (22). More recent analytical techniques have also been developed to allow researchers to conceptualise models that may provide insights and methods to better describe and compare growth and change

curves over time. Some of these life course methods provide new possibilities of modelling latent, pathway and cumulative effects in a conceptually coherent manner (23, 24).

Therefore, Chapter Six describes the results of using latent class analytical approaches to characterising latent BMI-for-age z-score trajectories using routine school-based health screening data from 1990 to 2011, and to determine whether educational transition from primary schools to secondary schools account for shifts in trajectories, and whether these patterns differ for boys and girls. This methodological approach provides deeper insights into the manner in which school-age children in Singapore are growing up in the past two decades. Identifying individuals as belonging to groups of distinct BMI trajectory characteristics early may provide both the individuals themselves and their health-care providers' opportunities to initiate early behavioural or other health promotion interventions better tailored to the specific group (25, 26).

Next, Chapter Seven adopts similar latent growth curve modelling techniques to determine the association of childhood and adolescent BMI Z-score trajectories as a determinant for later life health outcomes (26, 27). This study is a demonstration of how SLLCC can be linked with an existing National Health Survey 2010 dataset. The primary health outcome of this analysis is poor mental health status as measured by the General Health Questionnaire (GHQ-12), a self-administered screening tool designed to detect current mental disturbances and disorders (28). Findings from this study are particularly relevant, given the growing concerns about the rising epidemics of obesity and poor mental health, particularly when childhood obesity is both a risk factor and consequence of depression (29) and there are already concerns raised in Singapore (30, 31). In addition, the health implications of these global trends are

worrying, especially for children and adolescents considering that mental disorders are common in the general population, often have an early age-of-onset, and associated with significant adverse societal costs (29, 32).

In Chapter Eight, I summarise the key novel findings of the research and discuss its public health implications, particularly, in Singapore's context. Areas for future work are also proposed.

## Chapter 1: Background

### 1.1 BMI and early life predictors

In 2008, an estimated 1.46 billion adults (1.4–1.5) worldwide had a BMI of 25 kg/m<sup>2</sup> or greater, and of these 205 million men (193–217 million) and 297 million women (280–315 million) were obese with a BMI of 30 kg/m<sup>2</sup> or greater. Between 1980 and 2008, mean BMI worldwide increased by 0.4 kg/m<sup>2</sup> per decade (CI: 0.2–0.6) for men and 0.5 kg/m<sup>2</sup> per decade (CI: 0.3–0.7) for women (1).

The public health implications of this trend of increasing BMI globally since 1980 have been assessed by long-term follow up of large numbers of people. In 2009, a large collaborative analysis of 57 prospective studies with almost 900,000 adults, found that every 5 kg/m<sup>2</sup> increase in BMI was associated with about 30% higher all cause mortality (HR=1.29, CI: 1.27–1.32) and 40% higher ischaemic heart disease mortality (HR=1.41, CI: 1.37–1.45) (2).

Results from a meta-analysis pooling individual-level data from 26 observational studies from the Diverse Population Collaboration (mostly US and European countries) indicated that the risk of mortality for middle-aged adults with obesity (BMI  $\geq$  30kg/m<sup>2</sup>) was 22% higher than those with normal weight (BMI= 18.5–24.9kg/m<sup>2</sup>) (3). Among the elderly, a meta-analysis pooling 27 population-based cohort studies of people aged  $\geq$  65yrs old reported that the risk of all-cause mortality was 10% higher compared with those of normal weight (7).

Many studies that had described body weight as a risk factor or a predictor for mortality generally supported a quadratic or U-shaped relationship between BMI and death (33-36).

However, a systematic review of 40 cohort studies on the association between obesity, total mortality and cardiovascular events in patients with coronary artery disease, found that obese patients ( $\text{BMI} = 30\text{--}35\text{kg/m}^2$ ) had no increased risk for total mortality ( $\text{RR} = 0.93$ ,  $\text{CI: } 0.85\text{--}1.03$ ) or cardiovascular mortality ( $\text{RR} = 0.97$ ,  $\text{CI: } 0.82\text{--}1.15$ ) (37). Patients with severe obesity ( $\text{BMI} \geq 35\text{kg/m}^2$ ) did not have increased total mortality ( $\text{RR} = 1.10$ ,  $\text{CI: } 0.87\text{--}1.41$ ) but they had the highest risk for cardiovascular mortality ( $\text{RR} = 1.88$ ,  $\text{CI: } 1.05\text{--}3.34$ ) (37).

Obesity takes time to develop and excess weight takes time to lose. The risks of becoming obese start at an early stage. Accumulating evidence points to the detrimental effects of high BMI in childhood and early adulthood on later life morbidity and mortality (38, 39). A 1999 systematic review (40) has synthesised evidence on several domains of early life determinants namely, behavioural and psychological factors (13 papers from 10 studies), dietary factors (17 papers from 13 studies), genetic inheritance of phenotypes (3 papers from 3 studies), intra-uterine growth (20 studies), maturation (21 papers from 18 studies), physical activity (19 papers from 16 studies) and social factors (30 papers and 1 abstract from 21 studies). The authors argued that, although the associations may be subject to confounding, a number of childhood factors were predictive of later obesity; parental fatness, low social economic status (SES), higher birth weight, earlier/more rapid maturation and inactivity. There were several issues concerning interpretation of the interrelationships between risk factors: confounding, effect-modifiers and cumulative effects. Many of the suggested risk factors are highly correlated, or may operate as proximal and distal aetiological factors on the same causal pathways. Inherent problems in designing and measuring these risk factors made controlling for confounding, and



attempts to disentangle causal relationships between exposure risk factors and outcomes more difficult.

Consequently, more recent papers reflected that generally the understanding of the aetiology of obesity had not progressed much in the previous 10 years, especially in addressing confounding and it was still unclear whether the risk of morbidity associated with obesity varied with age of onset, severity, duration or the factors responsible for the onset (38, 41).

A systematic review of reviews (41) on the effects of early life determinants of overweight and obesity in under 5 years olds has shown that genetics, maternal factors, birth weight, infant size and growth, infant feeding, sleep duration, family, physical activity and sedentary behaviour, society and built environment are all associated with childhood obesity to different extents. However, the life course perspective was not emphasized, as seen from the absence of selection criteria relating to longitudinal studies, life course conceptual models and other classical life course research methodologies. Perhaps more stringent study selection criteria, such as including only longitudinal cohorts, should have been employed in this review because there is no other way to confidently determine causal relationships between early life determinants and later life obesity.

Several twin studies in children have confirmed that genetic factors influencing weight, BMI and body size become more apparent with age (42-45) despite an obesity-promoting environment (46). A recent study on obese children and their parents has shown that the influence of parental relative weight primarily affects the severity of their child's obesity and not

the timing; however, it is not clear whether the relationship between parental BMI and severity of obesity in their children was due to genetic or environmental factors (47). It is interesting however, to note that the correlation between parental BMI and severity of obesity in their children at age 15 became more pronounced suggesting that genetic factors may dominate later in life with decreasing parental impact on daily life.

In 2007, the UK Foresight (48) report adopted a systems mapping approach to gain insight into the biological and social complexities around the aetiology of obesity. The evidence gathered contributed to the development of a comprehensive causal model for adults based on the relative impact and size of the causal connections between 108 variables within and across 7 thematic clusters affecting energy balance in humans. The system map, together with scientific and other evidence, confirmed that energy balance (or imbalance) is determined by a complex multifaceted system of determinants (causes) and that no single influence dominates. Altering this complex system to tackle obesity will be far from straightforward.

However, it is important to note that the Obesity System Map was based on a causal model where temporal effects were less implicitly considered and it was not possible to establish temporal ordering or causal effects of these variables across the life course. Thus, new methods are required to help us understand the dynamics of developmental pathways and causal inference from longitudinal research on obesity.

Other issues that remain unresolved include: the mechanisms by which social-economic status (SES) in early life influences obesity in adulthood (49); whether the relationships between

birth weight and maturation and later obesity persist after accounting for confounding factors; whether any relationships between dietary factors and activity and excess weight in later life are due to a direct effect, or to tracking in dietary or activity behaviour; and how psychological factors and behaviours influence energy balance, and therefore degree of obesity.

A further neglected area of research is the identification of factors predicting the maintenance of a healthy relative weight, which may or may not be the opposite of predictors of obesity (40). The challenge to future research remains to discern which are the important and modifiable factors, or clusters of factors, and effects over time, on the causal pathway to the development of obesity.

Finally, one general shortcoming of previous research in this field is that quantification of the association of BMI as a risk factor for mortality has been principally based on severity or extent of overweight. Until recently, no study has examined the impact of the duration of obesity on the risk of mortality. Data from the original cohort study of the Framingham Heart Study suggested a dose-response relationship between years of duration of obesity with all-cause, cardiovascular, cancer and other-cause mortality (50) and diabetes (51). Middle-aged adults (aged 28 to 62) had a 50% increase in risk of death if they were obese for 1 to 5 years and for every additional 2 years of obesity, the rate increased by 6% (HR=1.06, CI: 1.05–1.07). For Type 2 diabetes, men had a 13% (HR=1.13, CI: 1.09–1.17) higher risk of type 2 diabetes and women a 12% (HR=1.13, CI: 1.08–1.16) higher risk per additional 2 years of obesity. The implications of this study are that prevention strategies need to delay onset of obesity and new research studies

need to consider duration of obesity when estimating future health burden associated with obesity trends.

## **1.2 Tracking of childhood overweight into adulthood**

A life course approach to chronic disease epidemiology involves the study of the long-term effects of physical and social exposures during gestation, childhood, adolescence, young adulthood and later adult life. Such an approach includes studies of the biological, behavioural and psychosocial pathways that operate across an individual's life course, as well as across generations, to influence the development of chronic diseases (52, 53). It offers new thinking to explore how socially patterned exposures during childhood, adolescence, and early adult life influence later adult disease risk and socioeconomic position, and hence may account for social imbalances in adult health and mortality. Socioeconomic factors at different life stages may operate either via social chains of risk or by influencing exposures to causal factors at earlier life stages that form part of long term biological or psychological chains of risk.

In the context of tackling adult obesity and chronic diseases, the life course approach is a growing area of research development fuelled by the increasing evidence of “tracking” or the maintenance of conventional risk factors from childhood to adulthood (54-56) and the evidence for “programming” as a potential model of disease aetiology, postulated by the Barker hypothesis on the developmental origins of health and disease (DOHaD) (8-10). In addition, emerging evidence indicates that some early risk factors may act across generations (57, 58).

In the epidemiological literature, there are two main aspects to “tracking”. The first is the relationship or correlation between early measurements and those later in life and second, the maintenance of a relative position within a distribution of values in the observed population through time or the predictability of future values by early measurements (59). Generally, it is commonly hypothesised that there are three main factors that might have contributed to the tracking patterns: a) chance or random measurement error, b) universal factors/ mechanisms that contribute to tracking in all individuals regardless of their initial status (called ‘common factors’); and c) unique factors/mechanisms that affect tracking among individuals with extreme values/ranking (60).

Tracking analysis is mostly used to evaluate the stability of the longitudinal development of risk factors for chronic diseases. However, before interpreting the results of tracking analysis, one has to be aware of the fact that the maintenance of a relatively high value of a risk factor over time may not be as important in predicting the development of a disease as a certain specific increase in the value of this risk factor (61). This holds true in the context of obesity, where low weight variability or stability is protective against increased relative risks of all-cause, cardiovascular disease (CVS) (62) and coronary heart disease (CHD) mortality (17).

Specific to the literature on tracking of childhood overweight and obesity into adulthood, a recent systematic review (55) concluded after considering 13 “high quality” studies out of 25 included studies, that the evidence on the likelihood of persistence of overweight into adulthood was moderate for overweight and obese youth, given that predictive values of future values varied considerably among studies. This observation is not surprising as one of the biggest

challenges in tracking analyses is the question of how to evaluate the magnitude of tracking, which is also highly dependent on the length of time interval between measurements (61).

Another way to better understand the childhood determinants of adult obesity is to understand the tracking of two key modifiable behaviours, food consumption and physical activity. Analysis reported in a 2011 systematic review (63) of both physical activity (28 papers from 16 studies) and dietary intake (11 papers from 5 studies) between childhood and adulthood found evidence of similar strength of tracking for both behaviours. However, given the diversity of study design and measurement methodology, it was challenging for the authors to obtain comparable estimates for variables such as actual food intake/usual eating habits. This supports the observation that the lowest tracking coefficients or tracking proportions are often found for variables with the highest measurement error (for variables with the lowest reproducibility (61).

Nevertheless, with respect to similar settings for this research, it is useful to highlight tracking studies conducted with large school-based datasets and nationally representative samples. For example, a six-year study of 16,245 Japanese students found that up to 70% of overweight/obese primary school children track into junior high school overweight/obese adolescents and the tracking is greater among boys than girls (64). The National Heart, Lung and Blood Institute Growth and Health Study in the US, a 10-year cohort study that recruited girls aged 9 and 10 years old at entry from public and parochial schools in Cincinnati, Ohio, indicated that changes in BMI during teen years are dependent upon childhood BMI levels and there is tracking of elevated BMI from ages 9 to 18 years of age. This is mainly due to greater

levels of BMI during childhood leading to greater than expected changes in BMI and disproportionate increases in fat mass especially after the pubertal growth spurt (65).

Tracking studies until now mostly employed probability approaches, where tracking is defined and measured as the probability of remaining in the same baseline category over time; or the use of tracking coefficients, such as Pearson and Spearman's correlation coefficients, Kappa and intra-class correlation coefficients. The third approach is the use of statistical models that can be fitted to predict future values from early measures (60). For example, a data-driven growth mixture modelling approach has been undertaken to explore patterns of BMI change across childhood and early adolescence in 182 non-Hispanic White girls in central Pennsylvania, US (66). By examining growth trajectories across both early and later childhood, the authors were able to illustrate that girls with accelerated weight gain during early childhood were not a homogeneous group but early accelerated weight gain was only associated with metabolic risk factors when that pattern persisted into adolescence.

### **1.3 Applicability of developmental trajectories to depict risk exposures**

Methodologically speaking, there are three main conditions that need to be met in order to infer a “causal effect” between two variables. Firstly, the presumed cause and effect are related, secondly, the presumed cause precedes the effect in time and thirdly, other competing explanations (confounding factors) can be ruled out (67). Thus, it is clear it is impossible to infer causality with cross-sectional studies. Therefore, the main challenge in most life course research of this nature is “how to infer causal inference” with prospective data in which the outcome of

interest in later life is the result of the entire trajectory of change in individuals across the life course.

Longitudinal studies use quite varied concepts for a trajectory of change (68). Briefly, most research questions relate to the timing of an event, for example, the age of onset of obesity or incidence of an acute fatal myocardial infarction. The probability that the event of interest will occur at time  $t$ , given that it has not already occurred, is called the “hazard” of the event. A person’s changing hazard is then that person’s trajectory. Another concept for analysing a trajectory of change has been described as a form of prediction of transitions between states, for example, if a person who has been obese will stay obese or cycle through being normal weight, underweight and overweight. A person’s trajectory is then characterised as the sequence of such transitions. Interest in this form of latent transition analysis (LTA) is best illustrated in studies investigating stages of change for smoking cessation (69) and in a 12-year longitudinal analysis of the development of childhood overweight, where four patterns of overweight across childhood were identified (70).

My research interest in this area was inspired initially by methods employed in developmental psychology (71, 72), where relationships between the different obesity trajectories and psychiatric disorders were specified in a latent growth model framework (73), in which probabilities of group membership can be derived. It may be, for example, that the predictors of being in an “always obese” or “early onset of overweight” group are quite different from the predictors of being in a “becoming obese” or “late onset of overweight” group. This



model thus seems especially useful when trajectories of change involve sets of parameters that mark qualitatively different kinds of development.

Similarly, researchers are often interested in whether or not and how parental social status may predict a person's educational attainment and how these variables, together, predict that person's adult occupation and income. A person's trajectory can then be characterised by the sequences of age-appropriate markers on the distal outcomes of interest. Common methods of analysis include structural equation models or path models. More complex techniques that describe and compare growth curves that describe a person's changing status have much relevance for this research, such as hierarchical modelling or multi-level modelling (24).

## **1.4 Rationale for research**

### **1.4.1 Obesity situation in Singapore**

Adult obesity ( $\text{BMI} \geq 30 \text{ kg/m}^2$ ) in Singapore increased over the last two decades, from 5.5% in 1992 to 10.8% in 2010 (21), which still represents one of the lowest prevalence rates among countries in the Asia region and in the Organisation for Economic Cooperation and Development (OECD) countries (74). However, National Health Survey 2010 findings within ethnic groups reveal obesity rates as high as 24% among Malays and 16.9% among Indians in Singapore. Similar patterns have been observed for age-standardised rates of abdominal fatness together with the highest BMI risks accrued to female Malays and Indians. Overall, 12.1% males and 9.5% females were obese.

As of June 2011, the racial breakdown of almost 5.2 million resident Singaporeans is 73% Chinese, 12% Malays, 10% Indians and 5% others. A cross-sectional study investigating BMI of Chinese, Malays and Indians in Singapore has shown that for males there were little ethnic differences, however, for females, Malays and Indians were significantly more obese than Chinese (75), consistent with the National Health Survey 2010 findings. Findings from the Singapore Cardiovascular Cohort Study (75) show that Indians had a three-fold increased relative risks of incident CHD (RR=3.1, CI: 2.0–4.8) compared with Chinese and Malays, after adjusting for age, ethnic group and other risk factors (LDL-Cholesterol, HDL-Cholesterol, triglycerides, BMI, smoking, diabetes, hypertension and alcohol use).

It is unlikely that BMI trajectories or trends over time would not be influenced by social disparities due to differential childhood social and economic status/positions (SES/SEP), commonly defined by highest educational level of the child's parent (76) or classification of parent's occupation (77) or income levels or type of housing. In the Singapore Malay Eye Study, lower SES, defined by categories of education and income were associated with higher prevalence of overweight/obesity in Malay women. In contrast, higher SES was associated with higher prevalence of overweight/obesity in Malay men (78). A prospective follow-up study of the 1998 National Health Survey on the socio-demographic determinants of changes in body weight and waist circumference in Singapore adopted highest education level, housing type and employment status as proxy measures for SES (79). Nevertheless, there is not yet a standard index of SES or SEP in Singapore. From the National Health survey 2010, the highest prevalence of obese individuals (BMI more or equal to 30.0kg/m<sup>2</sup>) occurred in households earning less than SGD 2,000 (about US\$1,582) per month (14.3%), compared to those earning

SGD 6,000 (about US\$4,746) or more per month (8.8%). Based on education level, a higher proportion of obese individuals were observed among those with Primary School Leaving Examination (PSLE) education or below (11.6%) when compared to those who had GCE 'A' Level education and above (9.7%) (80).

The prevalence of childhood obesity in Singapore has declined from 16.6% to 14.6% between 1992 and 2000 among primary 6 students (11 to 12 year olds). A similar decline has been seen in secondary 4 students (15 to 16 year olds) from 15.5% to 13.1% over the same period (81). However, within the last decade, based on BMI-for-age norms, there has been an increase in the percentage of overweight children at school entry age from the year 2000 (6.5%) to 2006 (7.8%). This has been followed by a slight decrease from 2007 (7.6%) to 2010 (7.4%). The percentage of overweight students also increased from primary 1 to primary 5/6, for both female and male students. However, the percentage of overweight children among primary 6 students decreased from 2008 to 2010, from 10.8% to 10.2% (82).

#### **1.4.2 Effect of weight change on later life**

Current evidence supporting the long-term effects of weight gain or loss (BMI changes) through the life course associated with risks in later life outcomes is unclear as previous systematic reviews were inconclusive in understanding the effects of life course weight changes on mortality. A 1993 systematic review on the association between weight loss and increased longevity (83) reported limited information on the magnitude of weight loss associated with changes in longevity and no information on the methods used to achieve weight loss, based on 6 primary observational epidemiological studies. A second systematic review on the long-term

effects of change in body weight on all-cause mortality (84), also in 1993, analysed 13 primary studies of weight change and presented evidence that some degree of weight gain during adulthood is associated with lower all-cause mortality. Both papers did not review the associations of weight changes with development of diseases or cause-specific mortality.

Any attempts to understand associations between weight change or fluctuations and mortality or morbidity is particularly challenging and requires sufficiently long term follow up in order to permit exclusion of early deaths so as to disregard likely effects of illness-related weight loss. This is often referred to as a “temporal separation” between periods of weight change measurements and of follow up for outcomes. Several other factors such as time period over which weight change is measured, methods used to define weight change, period of life during which weight change is measured, classification of body mass index, confounding by smoking, intentional weight loss and pre-existing morbidities, all make interpretations and comparisons of results from studies difficult.

There are also problems with statistical methods or research designs, especially for studies that only employ two time points. This type of weight change study is not ideal for studying development because the collection of individual trajectories is limited to a collection of straight lines. While two observations of BMI or equivalent measures such as waist circumference or waist-hip ratio provide information about the amount of change, they address other research questions quite poorly.

More recent analytical techniques have been developed to allow researchers to conceptualise models that may provide insights and methods to better describe and compare growth and change curves over time within a life span. Some of these life course research methods provide new possibilities to model latent, pathway and cumulative effects in a conceptually coherent manner (23). An appropriate life course statistical model is one that not only describes a single individual's developmental trajectory (in this case, BMI or weight), but also captures individual differences in these trajectories over time. If, for example, trajectories produced a collection of straight lines or nonlinear behaviour for a sample of individuals, the developmental model should reflect individual differences in the slopes and intercepts of those lines/curves (24). Another critical attribute of the life course model is the ability to study predictors of individual differences in order to answer questions about which variables exert important effects on the rate of development or change or growth. At the same time, the model should be able to capture the vital group statistics so that researchers can study development at the group level. One methodology with all these attributes is the latent growth model or LGM (85).

Given additional epidemiological studies since the last two systematic reviews in 1993, there is a need to critically re-appraise the strength of currently available evidence of the relative risks of weight changes (gain/loss/fluctuation) on all-cause mortality and mortality due to cardiovascular disease or coronary heart disease. Therefore, in my thesis, I intend to further investigate whether observed associations of weight change (gain/loss/fluctuation) with mortality are due to weight change *per say* or confounding by other factors.

### 1.4.3 Childhood and adolescence as critical periods

Given also that obesity is well known to track from childhood through to adulthood (54-56), and that the prenatal period, the period of adiposity rebound and adolescence represent critical periods for the development of obesity that persists into adulthood (86), it is important to understand the life course effects of growth changes and developmental trajectories in childhood and adolescence on obesity and other later health outcomes.

Several conceptual models have been developed to help elucidate the mechanisms underlying life course socio-economic position (SEP) effects on health (87). The accumulation model hypothesises that early and later adverse socio-economic experiences have a cumulative, dose-response effect on later outcomes (88). The latent model (or critical period) suggests that adverse socio-economic circumstances during childhood have an independent, detrimental effect on health, over and above current circumstances (87). Pathway models emphasise the importance of trajectories across the life course and are proposed if the influence of childhood SEP is attenuated after taking into account later conditions. Social mobility models are usually divided into intra-generational and inter-generational. Inter-generational mobility refers to a change in social class between generations, often measured by comparing parental social class to own social class in adulthood. Intra-generational mobility is the movement between different social classes in adulthood, such as the first and last occupation. No consensus regarding the health consequences of social mobility exists (89).

Previous research on the impact of early life developmental trajectories of overweight with later health outcomes had predominately focused on gestation weight, rapid weight gain in

early infancy or “catch-up growth” in the first two years of life, timing and peak of adiposity rebound around age 6 when BMI begins to increase following a nadir. Fewer studies concentrate on adolescence as a critical period for obesity, due to it being more temporally proximal to adulthood and thus less suitable for the application of interventions (90), from a life course statistical perspective, as there is only a short time period to determine independent causal effects of exposures during adolescence having a long-lasting impact in adulthood.

On the other hand, the distinct life stages of childhood from age 6 to 12, and adolescence from 12 to 18 have been regarded as key stages of human growth and psychosocial developmental (91). In this perspective, elementary school years from age 6 are deemed as critical for the development of self-confidence as children start recognising their special talents and continue to discover interests as their education improves. And from ages 12 to 18, the individual goes through a transition from childhood to adolescence. Demands and expectations for academic excellence in secondary or pre-college education may shape behaviour change and life-long habits for physical activity, diet, smoking and alcohol. This is also the life stage where most adolescents achieve a sense of identity regarding who they are and where their lives are headed (91).

To clarify, in life course epidemiology the relevance of changes during a critical period is regarded in respect of their long-term effects on disease risk many years later. Thus, for the purposes of this research, a “critical period” is defined as a limited time window in which an exposure can have adverse or protective effects on development and subsequent disease outcome (87). In other words, from a life-course perspective, a given risk factor exposure in early life may

modify the effect of another, and exert cumulative effects on the development of obesity and other later health outcomes, both over time for specific risks, or at any particular time over a range of risk factors.

This is why I would like to consider childhood and adolescent years as potential critical periods in influencing the development trajectories of growth.

### **1.5 Research aim and objectives**

In Singapore, the Singapore Health Promotion Board (HPB) assumes the role of the main driver for national health promotion and disease prevention programmes. Its goal is to increase the quality and years of healthy life and prevent illness, disability and premature death for Singaporeans (92). The School Health Service (SHS) and the School Dental Service provide preventive health care through immunisation, health and oral screening for children. The Student Health Centre provides clinic-based preventive and screening services for children who require further assessment following health screening in schools; for severely overweight and underweight students referred by Ministry of Education (MOE) schools; and for children who missed immunisation in school (92).

School health policies in Singapore are underpinned by the Championing Efforts Resulting in Improved School Health (CHERISH) Framework (93), which was instituted in year 2000. Modelled after WHO's Health Promoting School Framework (94), CHERISH encompasses aspects of healthy school policies, schools' physical and social environment,



community links, strengthening competencies for healthy living and the overall integration of school health services and health promotion activities.

In a monumental collaborative effort, the Ministry of Education (MOE), Ministry of Community Development, Youth and Sports (MCYS), Singapore Sports Council (SSC), together with Institute of Mental Health (IMH), Health Promotion Board (HPB), Singapore Heart Foundation (SHF), Changi General Hospital (CGH), KK Women's & Children's Hospital (KKH), Central Narcotics Bureau (CNB), Singapore Nutrition Dietetics Association (SNDA), National Institute of Education (NIE), Diabetic Society of Singapore (DSS) and Halogen Foundation have formed the Healthy Youth Committee (HY-Com) to look into improving and providing holistic health for all students. This encompasses the physical, social and mental health of young people (95). The inter-agency committee is now in its third term with the goal of to align the health promoting efforts of agencies, which have a stake in the health of our youths. HY-Com aims to provide a multi-faceted collaboration necessary to cultivate attitudes leading to the adoption of a healthy lifestyle in young people.

My PhD is sponsored by the Health Promotion Board and supported by the Ministry of Education and Ministry of Health with a broad goal to enhance the understanding of anthropometric development of children and adolescents in Singapore and its effects across the life course. The uniqueness of the thesis lies in the unprecedented access to data from two large national school health-screening programmes. Together, the datasets captured information routinely collected from school-based health screening of students in all primary schools (for

ages 7 to 12) and 95% of all secondary schools (for ages 13 to 16) in Singapore from 1990 to 2011.

The use of data-mining techniques has been shown to facilitate analysis of large amounts of available health services data collected by school nurses. Utilising routinely collected school-based data could aid our understanding of the child and adolescent obesity epidemic by demonstrating that BMI status is not static but rather, changes dynamically over time. For example, BMI data was collected and entered using an electronic tool by school nurses from 657,068 students attending 1,156 schools in 49 of 67 Pennsylvania counties and revealed that the vast majority of students across all grades K-12 and by school level who were normal weight remained in that category and some students, primarily in middle and high school grades, moved back in the desired direction from obese or overweight toward normal weight. Additionally, a few students moved from obese back to normal weight (96).

The overall aim of this thesis is to characterise anthropometric change among Singapore youth from 1990 to 2011 and explore relationships of their latent growth trajectories during childhood and adolescence on later health outcomes. This would be achieved through the following objectives:

1. To conduct a systematic review on effects of weight changes on all-cause and cause-specific mortality due to cardiovascular disease and coronary heart disease (**Chapter Two**)

2. To determine feasibility of and document procedures to establish a longitudinal cohort dataset by record linkages of repeatedly measured anthropometric data from routine annual school-based health screening in Singapore (**Chapter Three**)
3. To present an epidemiological profile of a new Singapore Longitudinal and Life-Course Cohort (SLLCC) that would be developed as part of this thesis (**Chapter Four**)
4. To investigate the possibility of a levelling of the obesity trend in Singapore and to explore age, period and cohort effects influencing obesity trends among school-age children in Singapore between 1997 to 2011 (**Chapter Five**)
5. To characterise latent BMI-for-age z-score trajectories using routine school-based health screening data from 1990 to 2011 (**Chapter Six**)
6. To explore associations of childhood and adolescent latent growth trajectories on later health outcomes in Singapore (**Chapter Seven**)

The final **Chapter Eight** will be a discussion and summary of the main findings from the thesis.

## **1.6 Data sources**

In this background chapter, a brief introduction of the three key data sources are described as more details are provided in Chapter Three: Data Sources and Preparation.

### **1.6.1 Health Promotion Board**

The first set of data for my research is the School Health Service (SHS) database from the Health Promotion Board. This dataset captures information routinely collected from an on-going

annual health screening dataset of school children in all primary schools (for ages 7 to 12) and 95% of all secondary schools (for ages 13 to 16) in Singapore. Data were computerised from 1990 to 2011 while paper archives were available for earlier years. Annually, about 44,000 new student records were added since 2000. In 2010, there were a total of 263,906 students in 173 primary schools and 214,388 students in 155 secondary schools (97, 98).

In SHS examinations, basic measurements (height & weight) were taken to calculate the student's height percentile, weight percentile, BMI, BMI percentile and growth velocity within the year cohort. Vision and audiometry tests were conducted as well as mandatory vaccinations. A primary physician conducted basic screening to check on heart, lung capacity as well as assessing the growth of the student, for example, puberty staging. A trained nurse determined weight and height.

Growth charts, by weight, height and BMI, for boys and girls from ages 6 to 18 were available for classification of weight status (92). The cut-offs were: youth with BMI scores falling  $\geq 97$ th Percentile were severely overweight; 90th to  $< 97$ th Percentile were overweight; 5th to  $< 90$ th Percentile were acceptable weight; 3rd to  $< 5$ th Percentile were underweight and  $< 3$ rd Percentile were severely underweight. It was also important to note that for the same amount of body fat as Caucasians who had a BMI of  $30 \text{ kg/m}^2$  (cut-off for obesity as defined by WHO), the BMI cut-off points for obesity would have to be about  $27 \text{ kg/m}^2$  for Chinese and Malays and  $26 \text{ kg/m}^2$  for Indians in Singapore. This was due to an observed paradox of low body mass index and high body fat percentage in the Singapore population (99, 100).

### **1.6.2 Ministry of Education**

The second set of data for my research is the Trim and Fit (TAF) database from the Ministry of Education. This dataset similarly captures information routinely collected from an annual health screening dataset of school children in all primary schools (for ages 6 to 12) and 95% of all secondary schools (for ages 13 to 16) in Singapore. However, data are computerised from 1997 to 2011 only.

Physical education teachers were trained to take basic measurements (height and weight) during TAF examinations using calibrated weight and height measurement machines. Students who were found to be underweight or overweight or obese were referred to the Nutrition Centre at the Health Promotion Board School Health Service centre for follow-up. In addition, those who were obese were enrolled into the TAF programme, as previously described.

### **1.6.3 Ministry of Health**

The main health outcomes data to be extracted from NHS 2010 respondents between age 36 and 46 in 2010 are obesity (based on height and weight) and mental health status. Briefly, among Singapore residents aged 18 to 69 years, 6.4% were underweight (BMI less than  $18.5\text{kg/m}^2$ ), while 53.5% had normal weight ( $18.5\text{--}24.9\text{kg/m}^2$ ) and 40.1% were overweight ( $\text{BMI} \geq 25.0\text{kg/m}^2 < 30.0\text{kg/m}^2$ ). One in nine (10.8%) Singapore residents were obese ( $\text{BMI} \geq 30.0\text{kg/m}^2$  or more) (21).

## **Chapter 2: Systematic review**

### **Synopsis**

Based on the initial scoping literature review in Chapter One, it is clear that there are negative effects of obesity on later life health outcomes in general and these have been well researched, while less is known about the impact of weight change itself, or patterns of weight change during childhood and adolescent on later life health outcomes including obesity. The scope of my thesis is to better understand how to evaluate life course effects of weight change, per say, on later health. Given that the last systematic reviews on this particular relationship were completed in 1993, this Chapter describes in detail the findings of a critical re-appraisal of the strength of currently available evidence of the relative risks of weight changes (gain/loss/fluctuation) on all-cause mortality and mortality due to cardiovascular disease (CVD) or coronary heart disease (CHD). Findings of this review would also help to identify methods used to characterise anthropometric change and evaluate the types of existing longitudinal studies of obesity around the world.

### **2.1 Introduction**

Body-mass index (BMI) is a reasonably good measure of general adiposity (101) and has been recommended by the International Obesity Task Force as the main measure of overweight and obesity in childhood and adolescence for survey purposes (102). Obesity is a well-known risk factor for the development of chronic diseases such as cardiovascular diseases and diabetes (103, 104). Relative to normal weight, obesity (all grades) is associated with significantly higher all-cause mortality (105).

Any attempt to understand associations between weight change and mortality or morbidity is particularly challenging and requires sufficiently long term follow up in order to permit exclusion of early deaths so as to disregard likely effects of illness-related weight loss. Several other factors such as time period over which weight change is measured, methods used to define weight change, period of life during which weight change is measured, classification of body mass index, confounding by smoking, intentional weight loss and pre-existing morbidities, all make interpretation and comparisons of results from various studies difficult.

It is therefore not surprising that the relative risk of weight gain on all-cause mortality can be challenging to interpret as both significant protective and non-protective effects have been identified. Several studies reported increased risks of 2% to 40% from large weight gain on all-cause mortality (17, 62, 106, 107). Others have reported protective effects of 11% to 36% (108-110) while some demonstrated little differences between those who gain the most weight versus having a stable weight (111, 112). Interpretation is further complicated by the lack of standardised weight categories even when comparing hazard ratios amongst those with greatest weight gain

In the context of adult obesity, weight change studies often attempt to investigate whether observed associations of weight change (gain/loss/fluctuation) with mortality are due to weight change *per se* or confounding by other factors. However, previous systematic reviews have been inconclusive in understanding the effects of earlier life weight changes on mortality. An early 1993 systematic review on long-term effects of change in body weight provided support for the concept that some degree of weight gain during adulthood may be protective on later life all-

cause mortality (84). Other reviews evaluating the association between weight loss and increased longevity have reported limited evidence for weight loss for either benefit or risk in relation to all-cause mortality (83, 113).

Given more recent epidemiological studies in the two decades since the 1993 systematic reviews, there is a need to critically re-appraise the strength of all currently available evidence of the relative risks of weight changes (gain/loss/fluctuation) on all-cause mortality and morality due to cardiovascular disease or coronary heart disease.

Briefly, my new systematic review is primarily interested in longitudinal studies conducted in healthy representative samples of the population, with serial measurements of weight/BMI using years of age as a time variable. There should be sufficiently long-term follow up in order to permit exclusion of early deaths so as to minimise likely effects of illness-related weight loss. BMI change categories or subgroups should be defined *a priori* in these cohorts and comparisons should be made at the end of the study between a reference category/subgroup that has the least change versus the others by use of relative risks (RR), hazard ratios (HR) or odds ratio (OR) with relevant confidence interval (CI) and p values reported.

## 2.2 Search strategy

Inclusion criteria:

- Longitudinal population cohort studies or trial studies that examined weight changes, effects of onset, severity and persistency of overweight and obesity across the life course



with relative risks of all-cause mortality and/or cause-specific mortality due to diabetes, cancer and cardiovascular diseases (for men and women and both children and adults)

- Cohort Studies investigating independent effect of weight change must define at least 2 weight categories (including reference/control category) with at least 2-measurement points within study period.
- Measures of fatness can include height & weight/Body Mass Index (BMI)/Body Adiposity Index (BAI)/waist & hip circumference ratio/ dual-energy X-ray absorptiometry (DXA) or other anthropometric measure to determine fat mass distribution. The use of fasting leptin (a hormonal measure of body fatness) can be included too.
- Participants must be healthy at baseline with absence of the outcomes of interest.
- The outcome of interest is first incidence of CVS/CHD or CVD/CHD mortality or all-cause mortality. For example, CVS may include pulmonary embolism, acute myocardial infarction and CHD may include narrowing of the blood vessels to the heart. Ideally, specific disease classification should be according to the International Classification of Diseases, any revision. (ICD-8 codes 400 to 444; ICD-9 codes 410 to 414; ICD-10 codes I21 to I28). Mortality should be determined by death certificates and coded with regard to underlying cause of death. Incidence should be physician diagnosed, either obtained from an official medical record/registry or self-reported.
- Only English language papers and abstracts published up to 6<sup>th</sup> August 2013 were considered for inclusion.

Exclusion criteria:

- Studies on effectiveness of interventions to reduce or control body mass index or fat mass (e.g. Randomised controlled trials)
- Participants with pre-existing conditions related to outcome measures and infants of very low birth weights
- Weight loss only studies
- No defined weight change categories
- Adult outcomes not relevant

The following online electronic databases were searched on 6<sup>th</sup> August 2013: Pubmed (1950 to 2013), EMBASE Classic + EMBASE (1947 to 2013), Global Health (1910 to 2013), HMIC Health Management Information Consortium (1979 to 2013), PsycEXTRA (1908 to 2013), PsycINFO (1806 to 2013), Econlit (1969 to 2013), Social Policy and Practice, Web of Science (1970 to 2013), BIOSIS Previews (1969 to 2013), Medline (1950 to 2013), Journals citation reports. The search term groups and Boolean logic steps are outlined below in sequence as an example.

Search terms:

- longitudinal or cohort or prospective or life course or lifecourse or birth cohort or case control or early life or critical period or early predictor or early determinant or accumulation risk or social mobility
- obes\* or overweight or over weight or abdominal or fat or fat mass or body mass index or BMI or BAI or adipos\* or hip circumference or waist circumference or waist hip ratio or

leg length or leptin or dual energy X-ray absorptiometry or weight chang\* or weight categor\*

- onset or severity or severe or persist\* or duration or intensity or cumulative obesity years
- weight chang\* or gain or loss
- cancer or diabet\* or cardiovascular or CVS or CVD or CHD or heart disease or heart failure or mortality
- survival model or structural equation model or sem or joint model or factor analysis or multivariate regression or cox model or latent class or latent effect
- (#1 and #2 and #3 and #4 and #5 and #6)

Another search strategy used combinations of keywords such as:

- (obesity OR bmi OR adiposity) AND longitudinal
- (obesity OR bmi OR adiposity) AND (life course OR lifecourse)
- (obesity OR bmi OR adiposity) AND critical period
- (obesity OR bmi OR adiposity) AND accumulation risk
- (obesity OR bmi OR adiposity) AND latent effect
- (obesity OR bmi OR adiposity) AND structural equation model
- (obesity OR bmi OR adiposity) AND multivariate regression model
- (obesity OR bmi OR adiposity) AND cox model
- (obesity OR bmi OR adiposity) AND causal pathway

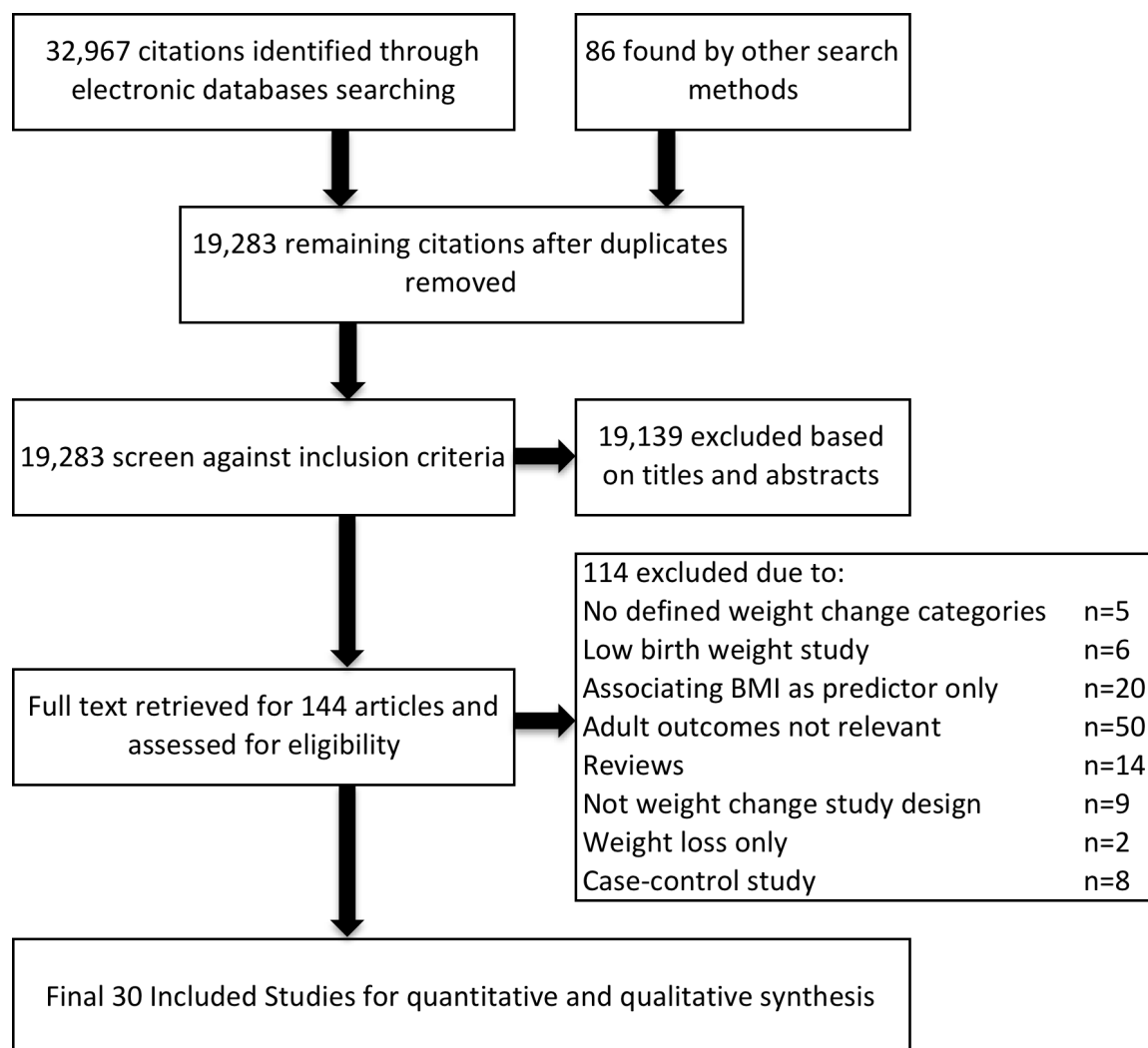
In addition, archives of three particularly relevant journals were searched separately:

International Journal of Obesity, Obesity Research & Clinical Practice and Obesity Reviews.

Finally, a search was conducted of the DARE database, the Cochrane database of systematic reviews and the Campbell Collaboration library to ensure that there were no previous systematic reviews done on this topic. An attempt was made to identify any potential on-going grants or past outputs on the Economic and Social Research Council (ESRC) UK research catalogue and none was found.

32,967 citations were first retrieved from electronic databases and 86 records were additionally selected from primary studies and bibliography of related systematic reviews on impact of early psychosocial factors on future risk of type 2 diabetes, metabolic disturbances and obesity (114), early life determinants of overweight and obesity (41, 115) and childhood obesity and adult cardiovascular disease risk (54).

The titles and abstracts of the 19,283 records, after removing duplicates, were screened against the inclusion/exclusion criteria and 19,139 records were excluded. Full text was then obtained for the remaining 144 articles for more detailed assessment of eligibility. Finally, 30 studies were included for quantitative and qualitative synthesis. Figure 1 shows the PRISMA flowchart, which depicted the process of selecting the final set of 30 included studies. I conducted the publication search and independently reviewed studies for eligibility.



**Figure 1 PRISMA flowchart of the systematic review on the association of weight change on all-cause and cause-specific mortality**

### 2.3 Data extraction process

Characteristics of included studies are shown in Table 1. All measurements in pounds were converted to kilograms for ease of comparison, where every 1-pound equals 0.45 kilograms. A separate comparison was made on the types of weight change study design,

comparing methods of expressing weight change, time between weight change periods, number of times weight measured and recalled, start and end ages/years of participants (see Table 2)

**Table 1 Characteristics of the studies (n=30) included in the systematic review on association of weight change with all-cause and cause-specific mortality (CVS/CHD)**

Reference	Study of Trial name (country)	Study size (M/F), average follow up	Outcome measures	Method of expressing weight change	Main Findings	Quality of Evidence <sup>a</sup>
<b>Blair, 1993</b>	Multiple Risk Factor Intervention Trial (US)	10,529 (M), 3.8 years	All-cause and CVS mortality	Weight variability	Men in 4th quartile by ISD <sup>b</sup> has increased risk for All-cause mortality (RR <sup>c</sup> =1.64, CI <sup>d</sup> : 1.21–2.23) and mortality from CVS (RR=1.85, CI: 1.25–2.75) compared to reference quartile.	Strong
<b>Breeze, 2006</b>	Whitehall cohort of male civil servants (UK)	4,862 (M), 5.4 years	All-cause and CVS mortality	Absolute weight change category and net BMI change	The net effect of weight change and BMI in middle age is that men with low BMI at one time and high BMI three decades earlier or later had the highest all-cause (RR=1.75, CI: 1.0–3.0) and CVD (RR=2.17, CI: 0.9–5.5) mortality rates.	Strong
<b>Dyer, 2000</b>	Chicago Western Electric Company Study (US)	1,281 (M), 25 years	All-cause and CVS mortality	Weight variability	Weight loss (RR=1.25, CI: 1.09–1.45) and weight gain (RR=1.14, CI: 0.76–1.33) were significantly related to 15-year CVS and all-cause mortality but weight variability was not. Results indicate that an association between weight loss and mortality may not persist beyond 15 years, and that weight variability may not be related to mortality independently of weight loss or weight gain.	Moderate
<b>Galanis, 1998</b>	Honolulu Heart Program (US)	6,176 (M), 17 years	Incidence of CHD	Absolute weight change category	Men who gained more than 2.5 kg between age 25 and examination I had a significantly higher risk of incident CHD compared with men in the stable category (RR=1.37, CI: 0.98–1.93), and this excess risk increased progressively across the weight gain categories. Weight loss over this period was not significantly associated with CHD risk. For the period of later weight change, in contrast, risk of CHD increased progressively	Moderate

					with weight loss.	
<b>Harris, 1997</b>	National Health and Nutrition Examination survey 1 (US)	1,581 (M/F), 3.9 years	Incidence of CHD	Absolute weight change category	Weight loss was associated with an increased risk of coronary heart disease for men (RR=1.9, CI: 1.2–3.1) and for women (RR=1.7, CI: 1.2–2.4). Weight gain was not associated with increased risk.	Strong
<b>Higgins, 1993</b>	Framingham Study (US)	2,500 (M/F), 20 years	All-cause and CVS mortality	Weight change category	Weight loss was associated with increased risk in men on all-cause (RR=1.33, CI: 1.06–1.68), CVS (RR=1.61, CI: 1.13–2.30) and CHD (RR=1.57, CI: 1.05–2.35) mortality. Lower risks are observed for women.	Strong
<b>Jeffreys, 2003</b>	Glasgow Alumni Cohort (UK)	629 (M), 35 years	All-cause and CVS mortality	BMI change category	Men who were overweight at both ages had greater than 2 fold risk of CVD mortality compared to men with stable normal weight (RR=2.56, CI: 1.15–4.71).	Weak
<b>Lee, 1992</b>	Harvard Alumni Health Study (UK)	11,703 (M), 12 years	All-cause and CHD mortality	Absolute weight change category	Risk for all-cause and CHD increased with both weight loss and gain more than 5kg. Weight change does not predict cancer mortality.	Moderate
<b>Lissner, 1991</b>	Framingham Study (US)	3,171 (M/F), 32 years	All-cause and CHD mortality	Weight variability	Men and women with highly variable body weights had increased all-cause and CHD mortality.	Strong
<b>Rimm, 1995</b>	Health Professionals Follow up Study (US)	29,122 (M), 3 years	CHD mortality	Absolute weight change category	No association between weight gain in adult life and coronary risk (after 1986) among men >65 years of age at baseline. Conversely, among younger men, those who gained 25-40 pounds (12-18 kg) after age 21 had increased relative risk for developing coronary heart disease (RR=2.12, CI: 1.18–3.78) compared with men who had not gained any weight.	Moderate
<b>Rosengren, 1999</b>	Multifactor primary prevention trial (Sweden)	6,874 (M), 20 years	All-cause and CHD mortality	Absolute weight change category	Compared with men who remained stable, men who gained more than 35% had higher relative risk of mortality from CHD (RR=2.76, CI: 1.97–3.85).	Strong



<b>Strandberg, 2009</b>	Helsinki Businessmen Study (Finland)	1,114 (M), 6 years	All-cause mortality	BMI change category	Mortality risk between 2000 and 2006 was not significantly different in those constantly overweight and among those men who turned overweight after midlife. The group with overweight in midlife but normal BMI in old age, in turn, had a significant two-fold increased mortality risk (RR=1.9, CI: 1.2–3.0) when compared with the constantly normal weight group.	Moderate
<b>Walker, 1995</b>	British Regional Heart Study (UK)	7,100 (M), 6.5 year	CHD mortality	Absolute weight change category	Relative risk of a heart attack was significantly increased only in men gaining most weight (RR=1.57, CI: 1.04–2.37).	Moderate
<b>Willett, 1995</b>	Nurses' Health Study (US)	115,818 (F), 14 years	Incidence of CHD	Absolute weight change category	Compared to a change of less than 5 kg, the risks for those who gained 20 kg or more was significantly higher (RR=2.65, CI: 2.17–3.22).	Moderate
<b>Hamm, 1989</b>	Western Electric Study (US)	1959 (M), 25 years	All-cause and CHD mortality	Absolute weight change category	Risk of CHD death in "gain and loss" group was doubled as compared with "no change" group (RR=2.0, CI: 1.2–3.5) and 50% higher for all-cause mortality (RR=1.5, CI: 1.0–2.3)	Strong
<b>Folsom, 1996</b>	Iowa Women's Health study (US)	33,760 (F), 6 years	All-cause and CVS mortality	Weight variability and Absolute weight change category	Women with greater weight variability, large weight lose (>10%) or a large cycle of weight change (>10%) had increased risks of CHD mortality compared to reference groups.	Moderate
<b>Diaz, 2005</b>	National Health and Nutrition Examination survey 1 and 1 Epidemiologic follow up (US)	8479 (M/F), 20 years	All-cause and CVS mortality	Weight variability and BMI change category	Weight fluctuation is associated with significantly increased risk in all-cause mortality (RR=1.83, CI: 1.25–2.69) and CVS mortality (RR=1.86, CI: 1.1–3.15).	Strong

<b>Yarnell, 2000</b>	Caerphilly Prospective Study (US)	2,512 (M), 18 years	All-cause and CHD mortality	BMI change category	Weight gain by middle age showed no clear relation with risk of subsequently CHD and all-cause mortality and the lowest mortality was found in men who had gained 16.1kg on average (RR=0.58, CI: 0.41–0.82)	Moderate
<b>Chou, 2013</b>	Ohsaki Cohort study (JP)	41,364 (M/F), 13.3 years	CVS mortality	Weight change category	In men, the multivariate-adjusted HR relative to the stable weight group was 1.52 (95% CI: 1.25–1.85) for the weight loss $\geq 10.0$ kg group, and no significant risks were observed in the other weight change groups. In women, the multivariate-adjusted HR relative to the stable weight group was (HR=1.62 CI: 1.25–2.11) for the weight loss $\geq 10.0$ kg group and (HR=1.36 CI: 1.09–1.69) for the weight gain $\geq 10.0$ kg group.	Strong
<b>Chei, 2008</b>	Japan Public Health Center-based prospective study (JP)	43 235 (M) and 47 444 (F), 11 years	CVS mortality	Weight change category	For men, weight gain was associated with 40% increased risk of coronary heart disease. Furthermore, weight gain $>10$ kg among men with BMI $< 21.4$ at age 20 years was associated with a twofold increased risk of coronary heart disease.	Strong
<b>Droyvold, 2005</b>	Nord-Trøndelag health study (NOR)	20 542 (M) and 23 712 (F), 5 years	All-cause and CVS mortality	Weight change category	There is no association between weight gain and mortality. People who lost weight had a higher total mortality rate compared with those who were weight stable (RR=1.6, CI: 1.4–1.8) in men and (RR=1.7, CI: 1.5–2.0) in women. Similar associations were found for cardiovascular and non-cardiovascular mortality.	Strong
<b>Myers, 2011</b>	Veterans Exercise Testing Study (US)	3,834 (M), 6.8 years	All-cause and CVS mortality	Weight change category	Weight gain was associated with lower mortality and weight loss was associated with higher mortality compared with stable weight. For all-cause mortality, the relative risks for the no change, weight gain, and weight loss groups were RR=1.0 as referent, RR=0.64 CI: 0.50–0.83, and RR=1.49, CI: 1.17–1.89.	Weak

<b>Stevens, 2012</b>	Cancer Prevention Study II Nutrition Cohort (US)	55,983 (M) and 66,655 (F), 16 years	All-cause and CVS mortality	Frequency of weight cycles	Low numbers of weight cycles (1–4 cycles) were associated with slightly lower mortality rates (HR=0.93, CI: 0.89–0.97) in men and (HR=0.93, CI: 0.89–0.98) in women, whereas high numbers of weight cycles (20 cycles) were not associated with mortality (HR=1.03, CI: 0.89–1.19 in men and (HR=0.99, CI: 0.88–1.12) in women.	Strong
<b>Peters, 1995</b>	Seven Countries Study (EU)	6441 (M), 15 years	All-cause and CVS mortality	Weight variability and Absolute weight change category	Significant elevated hazard ratios were found for all-cause mortality (RR=1.33, CI: 1.2–1.5) and CVS mortality (RR=1.24, CI: 1.01–1.51) for men with decreasing weight compared with men with a constant weight. A fluctuating weight was associated with an increased risk of all-cause mortality (RR=1.21, CI: 1.03–1.41) and myocardial infarction (RR=1.51, CI: 1.02–2.22).	Moderate
<b>Lee, 2011</b>	Aerobics Center Longitudinal Study (US)	14,345 (M), 11.4 years	All-cause and CVS mortality	Weight change category	BMI change was not associated with all-cause or CVD mortality after adjusting for possible confounders and fitness change. Each 1-unit increase of BMI was associated with a 1% and 6% higher risk of all-cause and CVS mortality respectively.	Strong
<b>Sauvaget, 2008</b>	Trivandrum Oral Cancer Study (IND)	49,216 (M/F), 3.5 years	All-cause mortality	Weight change category	A weight gain of 4–10% was related to a decreased mortality risk by 22 and 24% in men and women, respectively, as compared with a stable weight. Weight loss of 4–10% was associated with an increased risk of death (RR=1.38, CI: 1.07–1.79) in men and (RR=1.57, CI: 1.23–2.00) in women.	Strong
<b>Rzehak, 2007</b>	Erfort Male Cohort Study (DE)	505 (M), 15 years	All-cause mortality	Weight change category	Weight fluctuations are the main risk for all-cause mortality (RR=1.86, CI: 1.31–2.66). Weight loss reduces further survival as well. However, the effect of weight loss on mortality is mostly due to pre-existing cardiovascular disease or diabetes and the	Weak

					adverse health effects of smoking.	
<b>Wannamethee, 2002</b>	British Regional Heart Study (UK)	5,608 (M), 8 years	All-cause and CVS mortality	Weight change category	Sustained weight loss (or weight fluctuation showed significantly higher all-cause mortality risk than men whose weight remained stable. This is largely due to an increased risk of CVS mortality among these men. Weight loss and variability per se does not increase risk of mortality.	Strong
<b>Nguyen, 2007</b>	Dubbo Osteoporosis Epidemiology Study (AUS)	644 (M) and 1,059 (F), 13 years	All-cause mortality	Weight variability	While weight fluctuation increases risks of all-cause mortality in both men (RR=1.5, CI: 1.1–2.0) and women (RR=1.3, CI: 1.0–1.7), study shows that attributed risks caused by weight variability was about 1.4-3.4% as compared to rate of weight loss (11.6% in men and 10.9% in women).	Weak
<b>Iribarren, 1995</b>	Honolulu Heart Program (US)	6,537 (M), 14.5 years	All-cause mortality	Weight variability and BMI change category	Highest risk of all-cause mortality (RR=1.29, CI: 1.10–1.51) was associated with a weight loss of 2.6-4.5kg and CVS mortality with a loss of >4.5kg (RR=1.31, CI: 0.97–1.77) after fully adjusted. Men with highest weight fluctuation had the most risk of CVS (RR=1.41, CI: 1.03–1.93) and all-cause mortality (RR=1.25, CI: 1.05–1.48). However, these associations were not found among healthy men with never smoked.	Strong

## Notes:

<sup>a</sup> The quality assessment on included evidence is conducted using the Quality Assessment Tool for Quantitative Studies developed by The Effective Public Health Practice Project (EPHPP)

<sup>b</sup> ISD – Intra-personal Standard Deviation of weight is a measure of weight variability, where a subject's standard deviation of weight measurements taken at each examination is divided by the mean BMI of that subject across all examinations

<sup>c</sup> RR – Relative Risk

<sup>d</sup> CI – 95% confidence interval

**Table 2 Methods of expressing weight or BMI change in the 30 studies included in the systematic review of association of weight change with all-cause and cause-specific mortality**

Reference	Method of expressing weight or BMI change	Time between weight change period(s)	Number of times weight determined	Temporal separation (No. Of years)	Baseline age (period)	Study design <sup>a</sup>
<b>Blair, 1993</b>	<p>A) Intrapersonal standard deviation of weight (ISD)</p> <p>B) Type of weight change within 1 of 5 categories:</p> <p>1) No change was defined as a change of less than 5% from baseline at all visits;</p> <p>2) steady loss, as a loss greater than or equal to 5% of a previous weight that was not regained;</p> <p>3) steady gain, as a gain greater than or equal to 5% of a previous weight that was not subsequently lost;</p> <p>4) cycle with last change a loss, as a loss greater than or equal to 5% of weight that previously had been gained; and</p> <p>5) cycle with last change a gain, as a gain of 5% or more of weight that previously had been lost.</p>	50.8% subjects measured every 12 months and 49.2% every 4 months	6 or 18	7	35 to 57 years old (1973 to 1976)	4
<b>Breeze, 2006</b>	<p>Loss &gt; 10kg</p> <p>Loss 4 -9kg</p> <p>Loss 0-3kg or gain 0-3kg</p> <p>Gain 4-9kg</p> <p>Gain 10kg or more</p>	28.8 years (between first screening and resurvey)	2	2	40 to 69 years old (1968 to 1970)	1

<b>Dyer, 2000</b>	The slope of the regression line relating each man's BMI values to the time from baseline was computed to assess his yearly rate of change. Two additional slope variables representing weight loss and weight gain, respectively, were also computed to account for nonlinear associations between slope and mortality. The standard deviation of BMI and the standard deviation about the regression (RMSE), which assesses variation about the trend in BMI over the period, were computed as measures of weight fluctuation or variation.	Annually	5 to 8	15	40 to 55 years old (1957)	4
<b>Galanis, 1998</b>	Early weight change (25yrs to exam 1): Loss >5kg Loss 2.6 to 5kg Change within + 2.5kg (stable) Gain 2.6 to 5kg Gain >10kg	25 years	2	3	50 to 58 years old (1965-8)	2
<b>Galanis, 1998</b>	Late weight change (exam 1 to exam 3): Loss >2.5kg Loss 1.1 to 2.5kg Change within + 1.0kg (stable) Gain 1.1 to 2.5kg Gain >2.5kg	10 years	2	3	50 to 58 years old (1965-8)	1
<b>Harris, 1997</b>	Gain > 10% Gain or lose < 10% (reference stable) Loss > 10%	10 years	2	0	70 to 80 years old (1982-4)	1

---

<b>Higgins, 1993</b>	BMI change tertile: Loss No change Gain	2 years	5	4	35 to 54 years old (1954 to 1958) Exam 4	4
<b>Jeffreys, 2003</b>	Change in BMI: <1.5kg/m <sup>2</sup> 1.6 to 3.0kg/m <sup>2</sup> 3.1 to 4.5kg/m <sup>2</sup> >4.5kg/m <sup>2</sup>  Change in BMI early/mid adulthood: Stable normal weight Normal weight/overweight Stable overweight	15 years (between 1949 to 1963)	2	10	22 years old (1948-9)	1
<b>Lee, 1992</b>	Loss >5kg Loss >1kg <5kg Weight constant within 1kg Gain >1kg <5kg Gain >5kg	10 to 15 years (1962/66 to 1977)	2	5	42 - 47 years old (1962 to 1966)	1
<b>Lissner, 1991</b>	The coefficient of variation was defined as the standard deviation of BMI divided by the mean BMI for recalled weight at 25 and examinations 1 to 8	2 year	9	4	30 to 62 years old (1948)	5
<b>Rimm, 1995</b>	Loss >3kg Loss or gain 2kg Gain 3 to 6kg Gain 7 to 11kg Gain 12 to 18kg Gain >19kg	Recalled weight at age 21 to baseline in 1986	2	0	40 to 75 years old (1986)	2

<b>Rosengren, 1999</b>	Loss > 4% Stable weight of + 4% change Gain by 4 to 10% Gain by 10 to 15% Gain by 15 to 25% Gain by 25 to 35% Gain > 35%	Recalled weight at age 20 to first examination in (1970 to 1973)	2	0	47 to 55 years old (1970 to 1973)	2
<b>Strandberg, 2009</b>	BMI <25 both in 1974 and 2000 (constant normal weight) BMI >25 both in 1974 and 2000 (constant overweight) BMI < 25 in 1974 and >25 in 2000 (turning overweight) BMI >25 in 1974 and < 25 in 2000 (turning normal weight)	26 years	2	0	44 to 50 years old (1971-74)	1
<b>Walker, 1995</b>	Loss >10% Loss 4 to 10% Stable – gain or lose <4% Gain of 4 to 10% Gain >10%	5 years	2	0	40 to 59 years old (1978 to 1980)	1
<b>Willett, 1995</b>	Loss >20kg Loss 11 to 19.9kg Loss 5 to 10.9kg Loss 4.9 to gain 4.9kg Gain 5 to 7.9kg Gain 8 to 10.9kg Gain 11 to 19kg Gain >20kg	12 to 37 years (from age 18 to 1976 first examination)	2	0	30 to 55 years old (1976)	2
<b>Hamm, 1989</b>	Max gain and loss >10% Max gain >10% Max gain and loss <10% Max loss >10%	5 years	5	25	40 to 56 years old (1957)	5



<b>Folsom, 1996</b>	The standard deviation about the BMI regression of each person (root mean squared error method) with 4 quartiles of weight variability set.  Gain and loss >10% Gain and loss >5% <10% No change <5% from baseline Gain only >10% Gain only >5% <10% Loss >10% but maintained $\pm 5\%$ Other weight change patterns	10 to 15 years	5	0	55 to 69 years old (1986)	2
<b>Diaz, 2005</b>	Stable weight non-obese $\pm 3$ BMI units Stable weight obese $\pm 3$ BMI units Weight gain >3 BMI units Weight loss >3 BMI units Weight fluctuation (sum of deviations >5.04 pop mean)	5 to 6 years	5	0	25 to 74 years old (1971-74)	4
<b>Chou, 2013</b>	Loss $\geq 10.0$ kg Loss 5.0–9.9 kg Stable weight ( $\pm 4.9$ kg) Gain 5.0–9.9 kg Gain $\geq 10.0$ kg	Recalled weight at age 21 to baseline in 1994 (20-59 years)	2	3	40 to 79 years old (1994)	2
<b>Chei, 2008</b>	Weight lost No change Weight gain	Recalled weight at age 21 to baseline in 1990-3 (20-40 years)	2	0	40 to 69 years old (1990-3)	2
<b>Droyvold, 2005</b>	Weight lost Stable (a change in BMI <0.1kgm <sup>2</sup> ) Weight gain	11 years	2	0	20 to 55 years old (1984-97)	1

<b>Myers, 2011</b>	Weight lost Stable Weight gain	7 years	2	0	40 to 70 years old (1992- 2008)	1
<b>Stevens, 2012</b>	No. Of weight cycles: 0 1-4 5-9 10-19 ≥20	Variable	2	0	50 to 74 years old (1992)	6
<b>Peters, 1995</b>	Gain > 2kg Stable weight Loss >2kg Fluctuating (weight at 2nd examination >2kg or <kg than highest or lowest weight at examination 1 or 3)  Weight variability expressed by coefficient of variation around the mean (100 times the square root of the mean square error divided by the mean weight)	5 years	3	0	40-59 years old (1958- 1964)	4
<b>Lee, 2011</b>	BMI change per year categories: Weight loss (lower third of BMI change distribution) Stable (middle third) Weight gain (upper third)	6.3 years	2	3	30-50 years old (1974- 2002)	1
<b>Sauvaget, 2008</b>	Gain >10% Gain 4-10% Stable weight Loss 4-10% Loss >10%	3.5 years	2	3	37-65 years old (1995- 2004)	1

<b>Rzehak, 2007</b>	Stable weight non-obese $\pm 3$ BMI units	5 years	4	15	55-74	4
	Stable weight obese $\pm 3$ BMI units				years old	
	Weight gain $>3$ BMI units				(1973)	
	Weight loss $>3$ BMI units					
	Weight fluctuation (sum of deviations $>3.49$ BMI units)					
<b>Wannamethee, 2002</b>	Sustained gain ( $>4\%$ without any weight loss)	5 to 10 years	3	0	40-59	4
	Sustained loss ( $<4\%$ without any weight gain)				years old	
	Loss-gain (weight loss followed by gain)				(1983-	
	Gain-loss (weight gain followed by loss)				85)	
	Stable (less than 4% change in body weight)					
<b>Nguyen, 2007</b>	The coefficient of variation was defined as the standard deviation of BMI divided by the mean BMI (about 3%)	2 years	4	0	$>60$ years old (1989)	4
<b>Iribarren, 1995</b>	Loss $>4.5$ kg	3 years	3	5	50 to 58	4
	Loss 2.6 to 4.5kg				years old	
	Gain 2.5 to 4.5kg				(1965-8)	
	Gain $>4.5$ kg					
	5 quintiles of weight variability (coefficient of variation)					

Notes:

<sup>a</sup> This review identified six distinct study types which calculated weight change based on: 1) the difference in weight between two study examinations; 2) the difference between current weight and one or more recalled weight in young adulthood; 3) the differences between current weight and highest lifetime weight; 4) the trend of weight over a series of examinations; 5) the trend of weight over a series of examinations and one or more recalled weight in young adulthood; and 6) weight cycling (intentional and non-intentional).

A key difficulty in the assessment of risk of bias or quality was incomplete reporting (116). Tools for assessing quality in clinical trials are well described but much less attention has been given to similar tools for observational epidemiological studies, as in the case for this review (117). As this review did not include any randomised controlled trial, a quality assessment on included evidence using the Quality Assessment Tool for Quantitative Studies developed by The Effective Public Health Practice Project (EPHPP) was finally selected as it was a validated tool in public health research (118) and performed well when compared with the Cochrane Collaboration Risk of Bias Tool (119). Results of the quality assessment are presented separately for each set of outcomes (Table 3). This tool was used in conjunction with the EPHPP Quality Assessment Tool for Quantitative Studies Dictionary (118).

**Table 3 Quality assessment of evidence of the 30 studies included in the systematic review of the association of weight change with all-cause and cause-specific mortality using the EPHP tool**

Reference	Selection bias	Study design	Confounders	Blinding	Data collection	Withdrawals and dropouts
Blair, 1993	**	**	***	**	***	***
Breeze, 2006	**	**	***	**	**	**
Dyer, 2000	**	**	*	**	***	***
Galanis, 1998	**	**	*	**	***	***
Harris, 1997	**	**	***	**	***	***
Higgins, 1993	***	**	**	**	***	***
Jeffreys, 2003	*	**	*	**	*	***
Lee, 1992	**	**	*	**	**	***
Lissner, 1991	***	**	**	**	***	**
Rimm, 1995	***	**	*	**	***	***
Rosengren, 1999	***	**	**	**	**	***
Strandberg, 2009	**	**	*	**	**	***
Walker, 1995	***	**	*	**	***	***
Willett, 1995	***	**	*	**	***	***
Hamm, 1989	**	**	**	**	**	***
Folsom, 1996	*	**	***	**	**	***
Diaz, 2005	***	**	**	**	**	**
Yarnell, 2000	***	**	*	**	***	***
Chou, 2013	***	**	***	**	**	***
Chei, 2008	**	**	***	**	***	***
Droevold, 2005	***	**	***	**	***	***
Myers, 2011	*	**	*	**	*	**
Stevens, 2012	**	**	***	**	***	***
Peters, 1995	*	**	**	**	***	***
Lee, 2011	**	**	***	**	***	***
Sauvaget, 2008	**	**	***	**	***	**
Rzehak, 2007	*	**	**	**	***	*
Wannamethee, 2002	***	**	***	**	**	***
Nguyen, 2007	*	**	*	**	***	***
Iribarren, 1995	***	**	***	**	***	***

Notes:

\*\*\* Strong rating

\*\* Moderate rating

\* Weak rating

Finally, given the important differences between weight change categories or subgroups in each study, a separate table comparing adjustment for key confounding factors or baseline covariates are described in Table 4.

For visualisation of the relative risks (RR) of weight change versus reference group from primary studies, the fully adjusted RR and confidence intervals are presented in forest plots for every outcome of interest by type of weight change study design, quality of evidence and BMI/weight change categories/subgroups within included studies. These are reported in Tables 5 to 26.

**Table 4 Number of confounding factors adjusted for in the 30 studies included in the systematic review of the association of weight change with all-cause and cause-specific mortality**

Reference	Age	Sex	Smoking	Alcohol	Physical activity	Education	Social economic position	Diastolic blood pressure	Systolic blood pressure	Serum cholesterol	Use of medicines	Baseline BMI	Other factors
<b>Blair, 1993</b>	Y	Y	Y	Y	Y	N	N	Y	N	Y	Y	Y	None
<b>Breeze, 2006</b>	Y	N	Y	Y	Y	N	Y	Y	N	N	Y	Y	Pre-diagnosed heart attack, stroke, angina, diabetes, cancer, marital status
<b>Dyer, 2000</b>	Y	Y	Y	N	N	N	N	N	N	N	N	N	None
<b>Galanis, 1998</b>	Y	N	Y	N	N	N	N	N	Y	Y	N	Y	None
<b>Harris, 1997</b>	Y	Y	Y	Y	Y	Y	N	N	Y	Y	N	Y	Report of Diabetes, stroke and cancer
<b>Higgins, 1993</b>	Y	Y	Y	N	N	N	N	N	Y	Y	N	Y	Glucose intolerance, left ventricular hypertrophy
<b>Jeffreys, 2003</b>	Y	N	Y	N	N	N	N	Y	N	N	N	Y	Fathers social class, height
<b>Lee, 1992</b>	Y	N	Y	N	Y	N	N	N	N	N	N	N	Height at baseline
<b>Lissner, 1991</b>	N	Y	Y	N	Y	N	N	N	Y	Y	N	N	Glucose intolerance, slope and level of BMI
<b>Rimm, 1995</b>	Y	N	Y	Y	N	N	Y	N	N	N	N	Y	Total calories, vitamin E, family history of coronary heart diseases
<b>Rosengren, 1999</b>	Y	N	Y	N	Y	N	N	N	Y	Y	N	N	Diabetes

<b>Strandberg, 2009</b>	Y	N	Y	N	N	N	N	N	Y	N	N	N	Perceived health and self-reported of diabetes, memory disturbances, cerebrovascular disorders, coronary heart disease, congestive heart failure, pulmonary disease, musculoskeletal disease and cancer
<b>Walker, 1995</b>	Y	N	Y	N	N	N	N	N	Y	Y	N	Y	Recall of doctor diagnosis for hypertension and diabetes
<b>Willett, 1995</b>	Y	N	Y	N	N	N	N	N	N	N	N	Y	Menopausal status, current and past use of postmenopausal hormones, parental history of myocardia infarction before 60
<b>Hamm, 1989</b>	Y	N	Y	Y	N	N	N	N	Y	Y	N	Y	None
<b>Folsom, 1996</b>	Y	N	Y	Y	Y	Y	N	N	N	N	N	Y	Marital status, hormone replacement therapy, diabetes, hypertension, perceived health status
<b>Diaz, 2005</b>	Y	Y	Y	N	N	N	N	N	N	N	N	Y	Race, Charlson Comorbidity Index, perceived health status
<b>Yarnel</b>	Y	N	Y	N	N	N	Y	N	N	N	N	N	None
<b>Chou, 2013</b>	Y	Y	Y	Y	Y	Y	Y	N	N	N	N	N	None
<b>Chei, 2008</b>	Y	Y	Y	Y	Y				Y				History of diabetes
<b>Droyvold, 2005</b>	Y	Y	Y	Y	Y	Y	Y	N	Y	N	Y	Y	Marital status
<b>Myers, 2011</b>	Y	N	N	N	Y	N	N	N	N	N	N	N	Cardiovascular disease
<b>Stevens, 2012</b>	Y	N	Y	Y	Y	Y	N	N	Y	N	N	Y	Race, diet, weight change from 18 years old to 1982
<b>Peters, 1995</b>	Y	N	Y	N	N	N	N	N	N	N	N	N	Geographical region, BMI at 3 <sup>rd</sup> examination
<b>Lee, 2011</b>	Y	N	Y	Y	Y	N	N	N	N	N	N	N	Parental CVD, baseline BMI and maximal METs



<b>Sauvaget, 2008</b>	Y	Y	Y	Y	N	Y	Y	N	N	N	N	N	Religion, tobacco chewing
<b>Rzehak, 2007</b>	Y	N	Y	N	N	Y	N	N	N	N	N	N	Pre-existing diseases
<b>Wannamethee, 2002</b>	Y	N	Y	N	Y	N	Y	N	N	N	N	Y	Pre-existing diseases
<b>Nguyen, 2007</b>	Y	N	Y	N	N	N	N	N	N	N	N	N	Bone loss, CVD diseases, rate of weight loss
<b>Iribarren, 1995</b>	Y	N	Y	Y	Y	N	Y	N	N	N	N	N	Energy intake, pre-existing diseases

Notes:

Y – Factor adjusted for in model

N – Factor not adjusted for in model

## 2.4 Characteristics of Included Studies

Identifying the differential effects of weight change, fluctuation or variability, onset, persistence or duration of obesity was challenging, as these research objectives were often not among the original goals of established prospective cohorts concerned with cardiovascular disease, diabetes and cancer. Nevertheless, this review retrieved a total of 30 weight change studies with all-cause mortality and CVS/CHD mortality outcomes that met the selection criteria.

All papers were published in English after 1989 with many being long-term prospective cohorts in North America, Europe, Australia and Japan, of which only one was an intervention trial (62). Participants were mostly men, with only seven studies of mixed-gender (12, 16, 109, 120-123) and two large female-only cohorts (124, 125). Study sizes ranged from 629 to 115,818 participants with follow-up duration between 3 to 35 years (mean 13.6 and median 13.2 years).

Participants included in these studies were mostly from well established cohorts, such as the Framingham Study (US) and the Glasgow Alumni Cohort (UK) in the late 1940s; the Chicago Western Electric Company Study (US) in the 1950s; the Whitehall cohort of male civil servants (UK), the Honolulu Heart Program (US), the Harvard Alumni Health Study (UK) in the 1960s; the Helsinki Businessmen study (Finland), the British Regional Heart Study (UK), the Seven Countries Study (EU) and the Nurses' Health Study (US), the Aerobics Center Longitudinal Study (US), the Erford Male Cohort Study (DE) in the 1970s; and the National Health and Nutrition Examination Survey I (US), the Iowa Women's Health Study and the Health Professionals Follow-Up Study (US), the Dubbo Osteoporosis Epidemiology Study (AU) and the Nord-Trøndelag health study (NOR) in the 1980s. Studies were also conducted with

more recent cohorts such as the Ohsaki Cohort study (JP), the Japan Public Health Center-based prospective study (JP), the Veterans Exercise Testing Study (US), the Cancer Prevention Study II Nutrition Cohort (US) and the Trivandrum Oral Cancer Study (IND) in the 1990s.

There were several methods of expressing weight change or classifying types of weight change study design (107, 126). This review identified six distinct study types which calculated weight change based on: 1) the difference in weight between two study examinations; 2) the difference between current weight and one or more recalled weight in young adulthood; 3) the difference between current weight and highest lifetime weight; 4) the trend of weight over a series of examinations; 5) the trend of weight over a series of examinations and one or more recalled weight in young adulthood; and 6) weight cycling (intentional and non-intentional). One study (127) employed a Derived Weight Fluctuation Index, using six data points: weight when adult height was first reached, present weight, both maximum and minimum weight for the 3rd and 4th decade of life.

There were extensive study heterogeneities relative to the time period between weight examinations, varying from annual physical measurements to recalled weights from more than 40 years ago. Also, weight was measured an average of 3.1 times across the 30 studies (median was 2 times) and only 50% of the studies employed a temporal separation in their analyses. The mean period of temporal separation was 7 years with a median of 4 years (Table 2).

## 2.5 Quality of evidence

The global rating for each study was strong if there was no weak rating in any of the components assessed, moderate if there was only one weak rating and weak if there were two weak ratings. Of the 30 studies, 16 were rated as strong, 10 as moderate and 4 as weak. Details of the assessment using the EPHP tool are listed in Table 3.

In terms of selection bias, one study (35) based its findings on a subset of the Glasgow Alumni Cohort that comprised only 20% of the original cohort. Although, the authors reported no differences in mean age or mean BMI at baseline between those who were included and those who did not respond, there was no information on other important baseline characteristics and confounders such as childhood social class, weight history, and smoking for these two groups. Therefore, this study had a weak rating for this component.

In terms of study design, all included papers were prospective cohorts and non-randomised observational studies. Methods of randomisation and blinding were therefore neither assessed for bias nor appropriateness.

In terms of adjusting for confounding factors, a more detailed breakdown of ratings is provided in Table 4. Several studies (13, 14, 16, 33, 35, 106-108, 111, 124, 128-130) had a weak rating for this component due to lack of consideration of potential covariates such as age, smoking, alcohol use, physical activity levels, educational level, social economic position or income level, use of cardiovascular medications, baseline BMI, personal history of pre-diagnosed myocardial infarct, diabetes, cancer, dietary patterns, weight patterns and failure to

control for weight loss due to subclinical disease. Studies may introduce a major bias by adjusting for biologic effects of obesity such as increased blood pressure or total cholesterol as there is evidence showing that associations between adiposity measures and mortality may be partially mediated by these risk factors instead (131).

Tools adopted for collection of weight and height data varied among studies. In most cohorts, this information was collected at baseline and at each examination. Depending on the type of weight change study design, recall of weight earlier in life, for example, at the age of 18, 20 or 25, were either self-reported via surveys, and/or guided by the use of somatotypes or diagrams representing human sizes ranging from extreme thinness to obesity. For studies with physical examination by trained personnel, height and weight were usually determined using appropriate weight scales and tools. In some studies, additional body measurements were taken such as waist circumference and waist-hip ratios.

An open-sourced software (132) was used to construct forest plots of hazard ratios comparing subgroups of people with different weight change histories against all-cause, CVS/CHD mortality and first incidence of CHD. The stratification of forest plots by study design types, EPHPP ratings, outcomes, and subgroups of greatest weight gain, loss or fluctuation allowed convenient visualisation to support further qualitative critique of various perspectives on the review findings. However, a meta-analysis calculation of combined effect sizes is not included due to high heterogeneity of study populations; definitions of weight change measures; use of control groups and sub-population segmentations; data collection methods; type

of weight change study design, adjustment of confounders, covariates, mediating factors, and statistical methods employed.

## **2.6 Main findings**

### **2.6.1 All-cause mortality**

23 studies evaluated the impact of weight changes on all-cause mortality (Table 1). The forest plots show relative risks (RR) of all-cause mortality with lower and upper limits of its confidence interval (CI) by each weight change category within each study when compared with a reference category (usually minimal change or least weight variability). The studies were grouped by weight change study design type (1 to 6) in order to compare within and between types.

#### ***2.6.1.1 Difference in weight between two study examinations***

Five of the eight studies (Table 5) that compared the difference in weight between two study examinations (study type 1) showed a “J-shaped” or “U-shaped” relationship, where relative risks for all-cause mortality increased with both weight loss and gain (33-36) except in a prospective study of adult men and women from rural India where it is more likely that severe weight loss is related to a high risk of mortality while a moderate weight gain showed a protective effect for all-cause mortality (110). The association of weight loss with increased mortality was also observed in the Veterans Exercise Testing Study (US) (108) and an established cohort in Norway, where the latter study further suggested that weight change is associated with a more unfavourable relative change in fat-free mass in men than women (133). Although the sequence of events for weight change and disease-onset was not directly measured

in one study (34), it was considered that reverse causation seemed less likely given that BMI change continued to predict mortality in the third–fifth years of follow-up. Other limitations may include the fact that data were unavailable as to whether weight loss was involuntary or intentional (33) and that self-reported weight in mid adulthood was used in the analysis and there are small numbers in the second examination compared to baseline (35).

Recent research from the Aerobics Center Longitudinal Study (US) (112) investigated the combined effects of cardiovascular fitness and BMI and concluded that BMI change was not significantly associated with all-cause mortality and the observed risk of CVS mortality associated with BMI gain was no longer significant once fitness change was taken into account, indicating modification of effect by fitness change on the association between BMI change and CVS mortality. The implication that men who lost fitness had a higher mortality risk regardless of BMI change compared with the reference group (men who improved fitness and decreased BMI), is important as most studies of BMI/weight change and mortality do not take fitness into account.

In the longitudinal cohort of the Helsinki Businessmen Study, mortality risk was not significantly different in those constantly overweight and among those men who became overweight after midlife. The group with overweight in midlife but normal BMI in old age, in turn, had a significant two-fold increased mortality risk ( $RR=1.9$ ,  $CI: 1.2–3.0$ ) when compared with the constantly normal weight group (111). These findings may suggest cardiovascular aetiology for developing frailty and give one explanation for the obesity paradox by showing that in old age both normal weight and overweight groups are actually mixtures of men with different

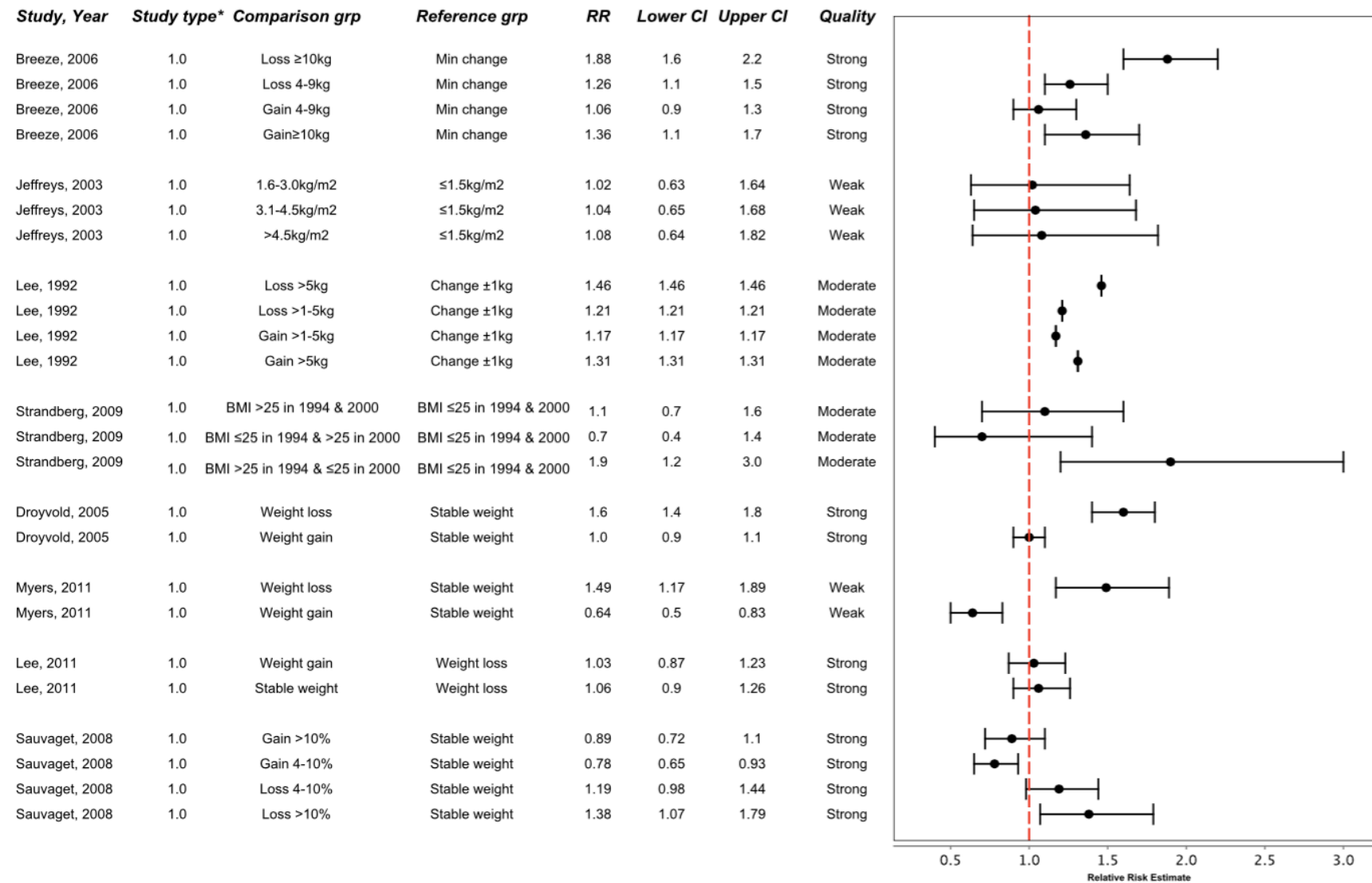
weight and cardiovascular risk histories. One limitation of this study and explanation for this observation by the author was that the small differences in mortality risk from old age onwards between the overweight groups and constantly normal weight group may be due to a relatively short follow-up of 7 years. The overweight groups may just be entering the weight loss (frailty) phase and their characteristics in the later years suggested that the prognosis would probably worsen during more extended follow-up.

#### ***2.6.1.2 Differences between current weight and one or more recalled weights***

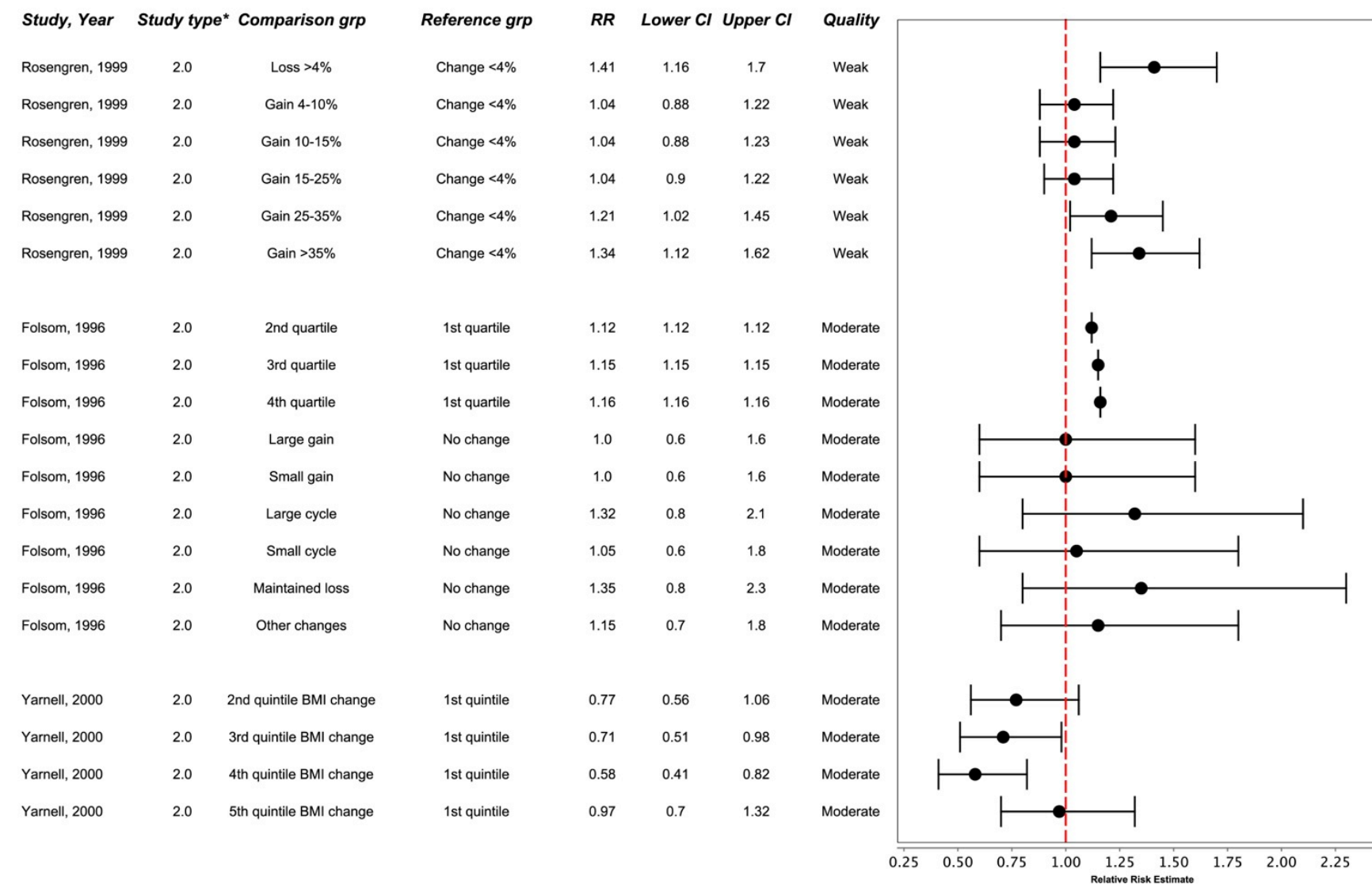
Three studies (106, 125, 134) examined the difference between current weight and a recalled weight in young adulthood (Table 6). The Multi-factor Primary Prevention Trial (Sweden), compared with men who remained stable, men who gained more than 35% of their baseline weight had higher relative risk of mortality from CHD (RR=1.86, CI: 1.32–2.62). A similar level of risk was also observed for men who lost more than 4% of their baseline weight. Findings from the Iowa Women's Health study (US) and the Caerphilly Prospective Study (US) on the lack of association between steady weight gain during middle age with risk of subsequent CHD and all-cause mortality were similar. However, the former study found that women with large weight loss (>10%) or a large cycle of weight change (>10%) had increased risks of CHD mortality compared to reference groups (125), whereas the lowest mortality was found in men who had gained 16.1kg on average (RR=0.58, CI: 0.41–0.82) (134).



**Table 5 Forest plots comparing Included Studies that measured the difference in weight between two study examinations (study type 1) for the association between weight change with all-cause mortality**



**Table 6 Forest plots comparing Included Studies that measured the difference between current weight and one or more recalled weight in young adulthood (study type 2) for the association between weight change with all-cause mortality**



### ***2.6.1.3 Trend of weight over a series of examinations with or without a recalled weight***

11 studies analysed the effect of weight variability or fluctuation over a series of examinations (study type 4), including two studies that incorporated one or more recalled weights (study type 5) (Table 7). General observations include a linear trend of increasing variability associated with increasing risk of all-cause mortality in one study (62) and for studies that compared later life mortality relative risks between a single sub-group of individuals with weight fluctuation versus a stable weight reference group, a common finding was increased mortality risk with this form of weight change pattern (12-18). Only one study reported a “U-shaped” relationship for all-cause mortality risk with individuals who have either experienced lowest or highest weight fluctuation in earlier life (135) and one study did not find any association of weight variability with risks of all-cause mortality in later life (107).

In the Multiple Risk Factor Intervention Trial study (62), men in 4th quartile by intra-personal standard deviation of weight (ISD) (highest weight variability) had increased risk for all-cause mortality (RR=1.64, CI: 1.21–2.23) and mortality from CVS (RR=1.85, CI: 1.25–2.75) compared to reference quartile (least weight variability).

For the Framingham Heart Study, there were two studies both analysing trend in weight over a series of examinations, including one with an additional recalled weight at age 18 (17). The first study (109) found evidence that weight loss was associated with increased risk in men on all-cause (RR=1.33, CI: 1.06–1.68), CVS (RR=1.61, CI: 1.13–2.30) and CHD (RR=1.57, CI: 1.05–2.35) mortality. Lower risks are observed for women. The second study (17) showed that

men and women with highest variable body weights in this cohort had increased all-cause (RR=1.65, CI: 1.32–2.06) and CHD mortality compared with those with least changes.

In the Chicago Western Electric Company Study (US), weight loss (RR=1.25, CI: 1.09–1.45) and weight gain (RR=1.14, CI: 0.76–1.33) were significantly related to 15-year CVS and all-cause mortality but weight variability was not. Results indicate that an association between weight loss and mortality may not persist beyond 15 years, and that weight variability may not be related to mortality independently of weight loss or weight gain (107). In this study, the correlation between the standard deviation of BMI and the slope was 0.08 when the direction of the trend in weight was ignored. However, the correlation was –0.77 in men who lost weight (negative slope) over the period and 0.75 in men who gained weight (positive slope). These high correlations with weight loss and weight gain make it difficult to assess whether an association of variability with increased mortality is a true association or rather reflects associations of weight loss and/or weight gain with mortality (107).

The Honolulu Heart Program (US) study addressed the important question of whether observed associations of weight changes, including variation, with mortality are due to effect of underlying disease or to confounding by other factors, especially within men who smoked cigarettes. Stratified analysis showed that the strongest association between the top quintile of weight variation and death from cardiovascular disease was observed among smokers with existing disease. Conversely, large variations in weight were unrelated to death from cardiovascular disease among healthy men who had never smoked. Similarly, large weight variations were a statistically significant risk factor for death from non-cardiovascular and from

all causes in smokers who were free of disease and were a non-significant factor among those free of disease, who had never smoked (135).

#### **2.6.1.4 *Weight cycling***

Weight cycling, referring to the repeated loss and regain of weight, has also been hypothesised to be a factor for obesity and to have effects on metabolism, morbidity, mortality and psychological well being. In 1994, the National Task Force on the Prevention and Treatment of Obesity commissioned a systematic review to address concerns about the effects of weight cycling and concluded that the evidence regarding long-term health effects of weight cycling is lacking (136). Subsequent reviews had similarly pointed out that such weight cycling may have different causes and effects in obese and non-obese individuals, however study design strategies used to define and evaluate weight cycling vary markedly (19) and findings from limited large-scale studies were still insufficient to alter public health recommendations regarding weight control (20).

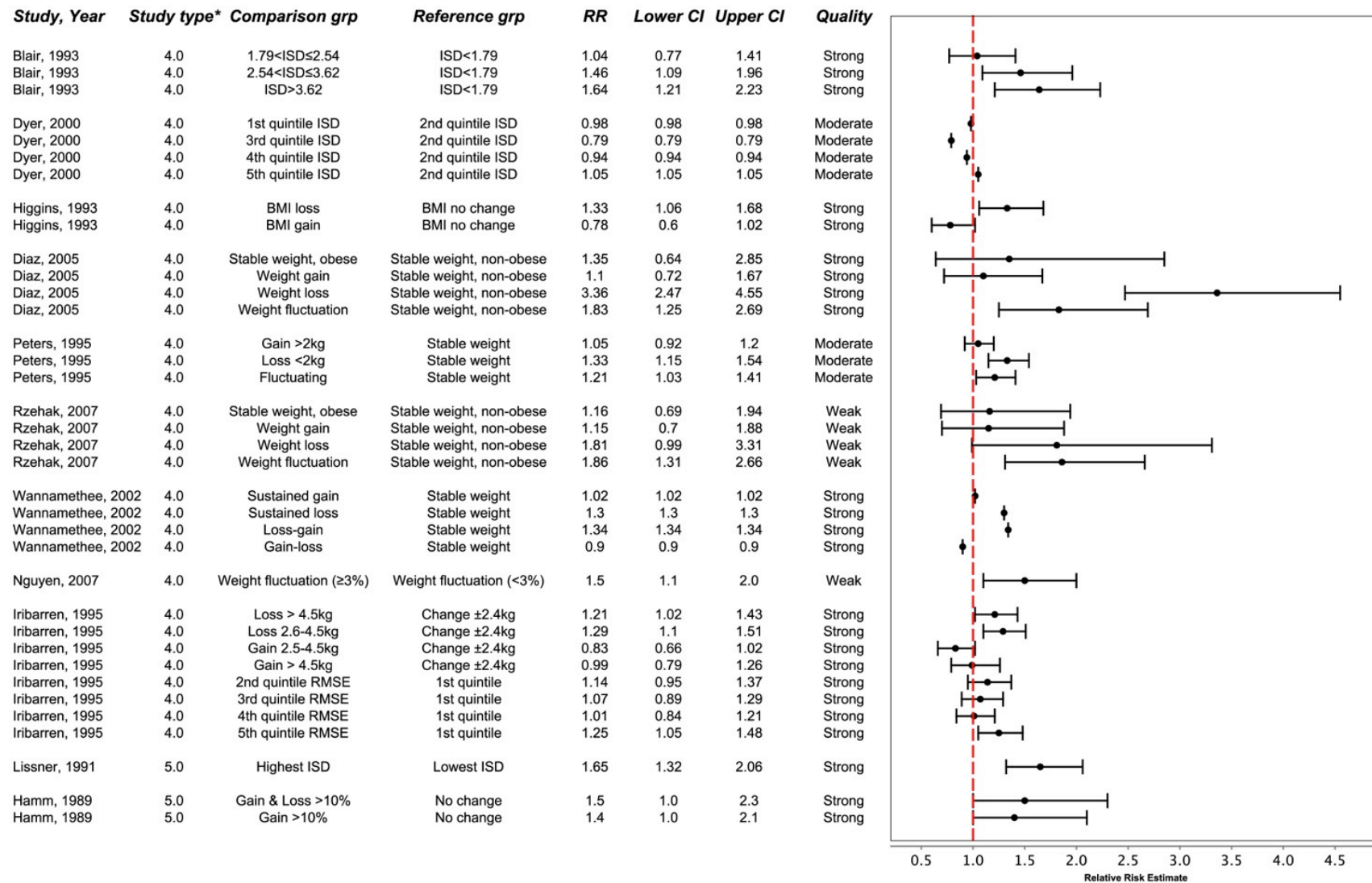
The majority of previous systematic reviews (19, 20, 136) on weight cycling retrieved studies that were small scale (average size=40 participants) and were mostly evaluations of dieting programs, except for one which investigated weight variation in the Baltimore Longitudinal Study of Ageing (n=846) and the Rancho Bernardo Cohort (n=1,900), which analysed self-reported weight change between ages of 40 and 60 years.

In the context of this systematic review, weight cycling was regarded as intentional or purposeful weight loss and subsequent weight gain, defined as one cycle. Two papers were

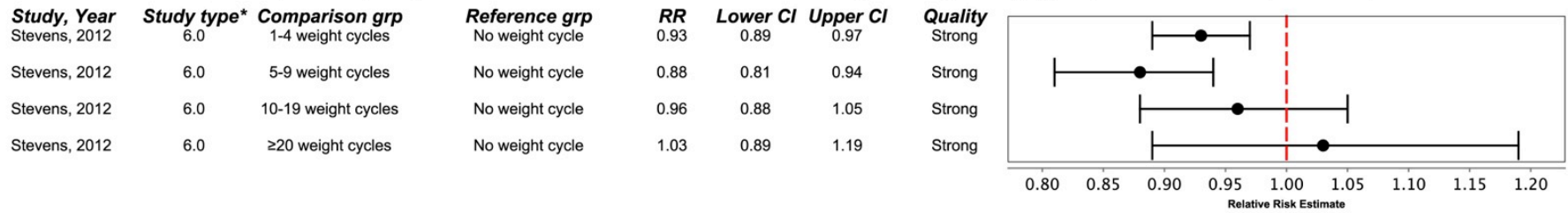
excluded due to being weight-loss only studies (83, 137) and finally, only one study on weight cycling that met all inclusion criteria was identified (121) (Table 8).

In the large Cancer Prevention Study II Nutrition Cohort (US), 55,983 men and 66,655 women were followed up for 16 years to investigate the association between the frequency of weight cycles and all-cause and CVS mortality. The study found that low numbers of weight cycles (1–4 cycles) were associated with slightly lower mortality rates (HR=0.93, CI: 0.89–0.97 in men and HR=0.93, CI: 0.89–0.98 in women), whereas high numbers of weight cycles (20 cycles) were not associated with mortality (HR=1.03, CI: 0.89–1.19 in men and HR=0.99, CI: 0.88–1.12 in women). Unique to this study is the attempt to determine whether the association between weight cycling and all-cause mortality varied by BMI in middle age and by weight change between age 18 and middle age. No change in the associations was reported and being a smoker did not attenuate this. This study, like most others, did not collect or consider information on the timing of onset, severity and duration of each weight cycle.

**Table 7 Forest plots comparing Included Studies that measured the trend of weight over a series of examinations (study type 4) with one or more recalled weight in young adulthood (study type 5) for the association between weight change with all-cause mortality**

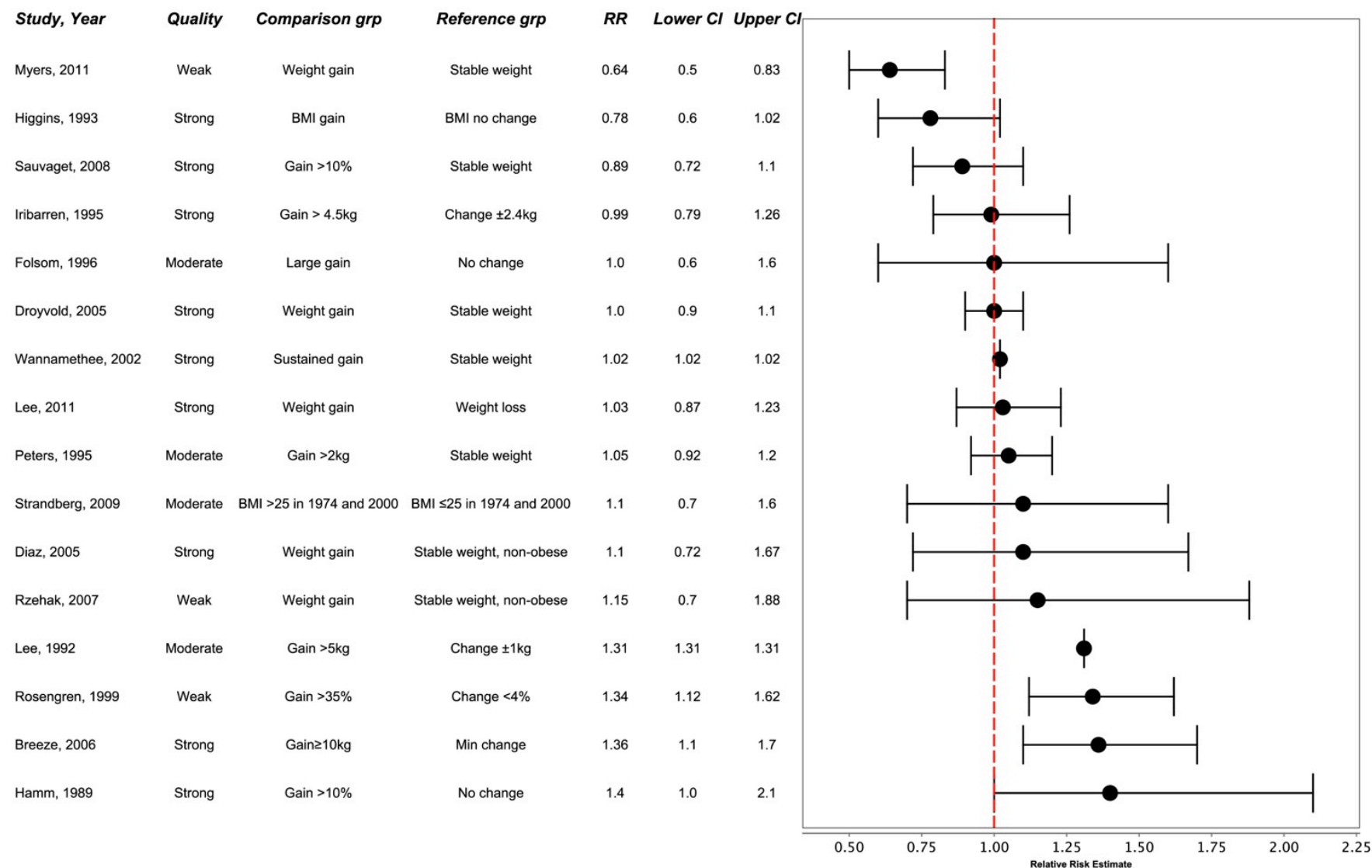


**Table 8 Forest plots comparing Included Studies that measured weight cycling (study type 6) for the association between weight change with all-cause mortality**

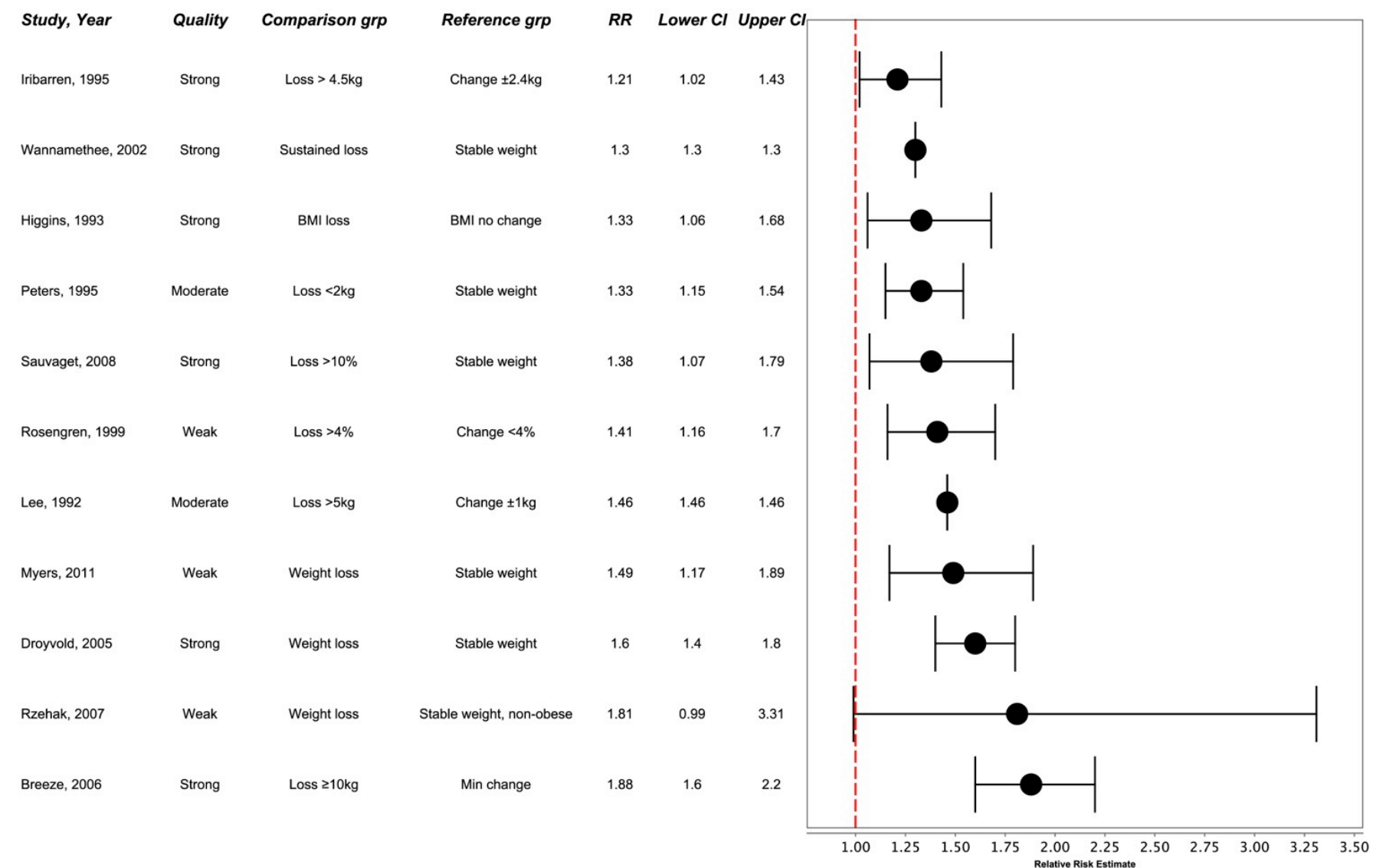




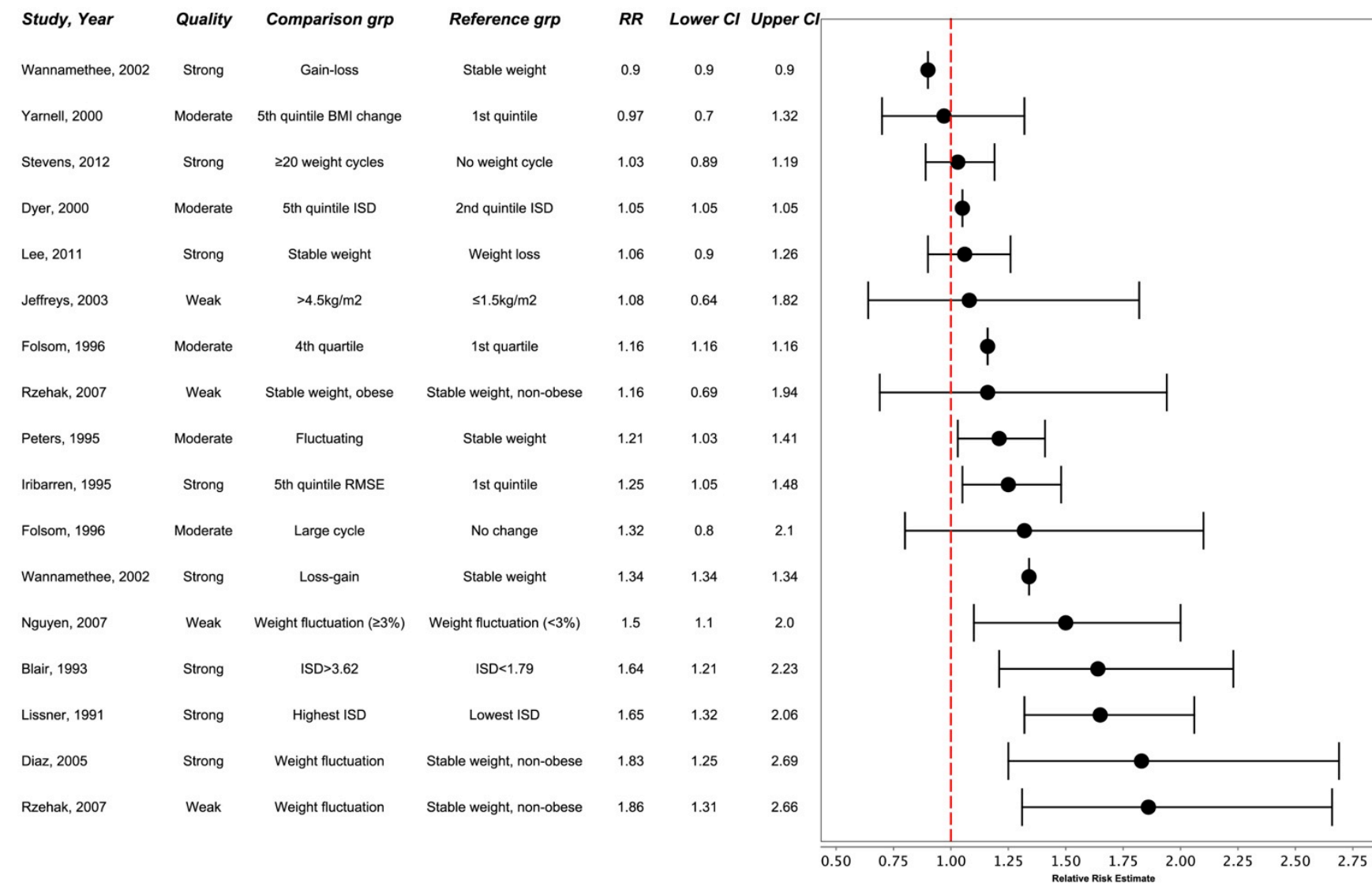
**Table 9 Forest plots comparing Included Studies on the relative risks associated between subgroups of greatest weight gain versus reference group with all-cause mortality**



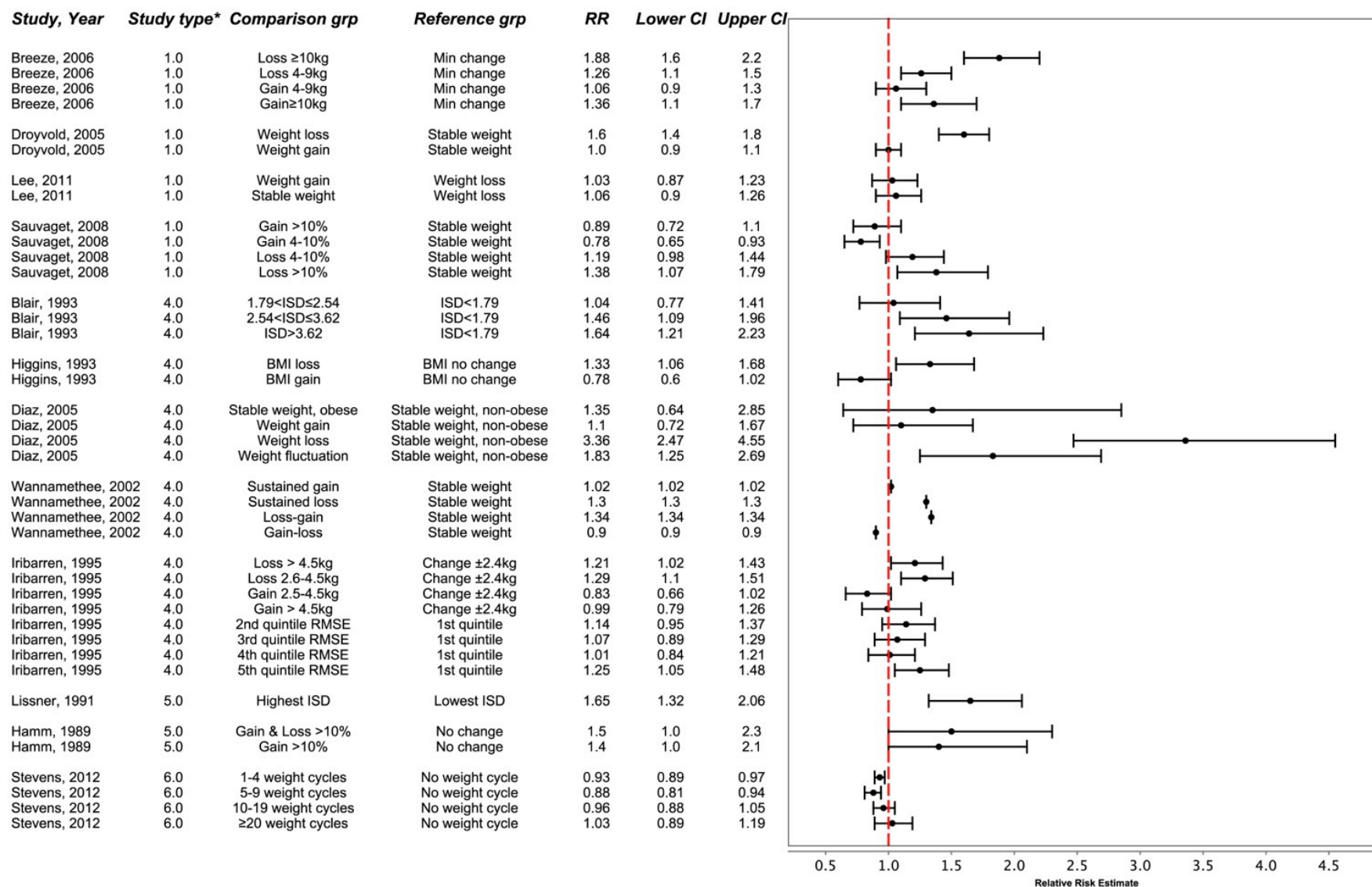
**Table 10 Forest plots comparing Included Studies on the relative risk associated between subgroups of greatest weight loss versus reference group with all-cause mortality**



**Table 11 Forest plots comparing Included Studies on the relative risk associated between subgroups of greatest weight fluctuation versus reference group with all-cause mortality**



**Table 12 Forest plots comparing Included Studies with Strong EPHPP evidence rating for the association between weight change with all-cause mortality**



## 2.6.2 CVS morality

14 studies evaluated the impact of weight changes on CVS mortality (Table 13, Table 14, Table 15, Table 16 and Table 17). Findings from the Whitehall Cohort of male civil servants (34) showed a “U-shaped” relationship between increased relative risks with both weight loss (RR=1.92, CI: 1.5–2.5) and weight gain (RR=1.8, CI: 1.3–2.9) on CVS mortality. The Glasgow Alumni Cohort (35) had the same study design although the method of expressing weight change was non-comparable as it used both change in BMI reflecting magnitude of variability, and the type of weight change (gain or lost) but without absolute weights. Limited information could be obtained from this study beyond the observation that men who were overweight in both early and mid-adulthood conferred a two-fold risk (RR=2.33, CI: 1.15–4.71) compared to those who remained stable normal weight and contrary to previous studies (17, 62, 107), weight variability was not associated with all-cause or CVS mortality.

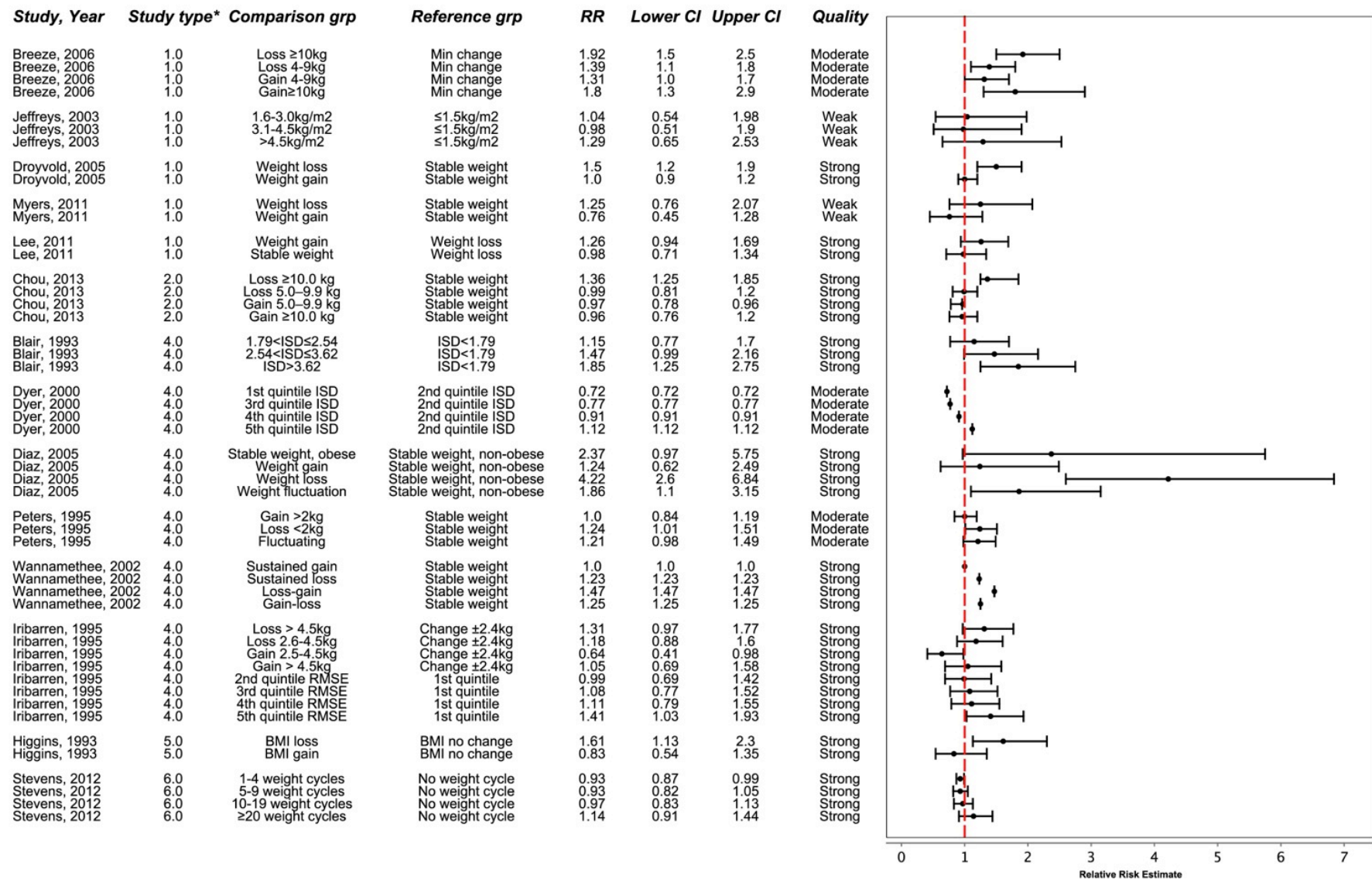
Findings for weight loss on CVS mortality relative risks were consistent across studies conducted with the Nord-Trøndelag health study (NOR) (133), the Veterans Exercise Testing Study (US) (108) and the Ohsaki Cohort study (JP) (123) where weight loss of more than 10kg conferred an increased relative risk of 1.25 to 1.5 as compared to maintaining a stable weight.

Similar findings are seen in several studies where men whose weights remained stable were at the lowest adjusted risk of CVS mortality, as described for all-cause mortality, compared with those whose weight changed the most (12, 13, 62, 107). In the British Regional Heart Study (UK) sustained weight loss or weight fluctuation was associated with significantly higher all-cause mortality risk compared with men whose weight maintained stable. This is largely due to

an increased risk of CVS mortality among these men as weight loss and variability *per se* does not increase risk of mortality (15).

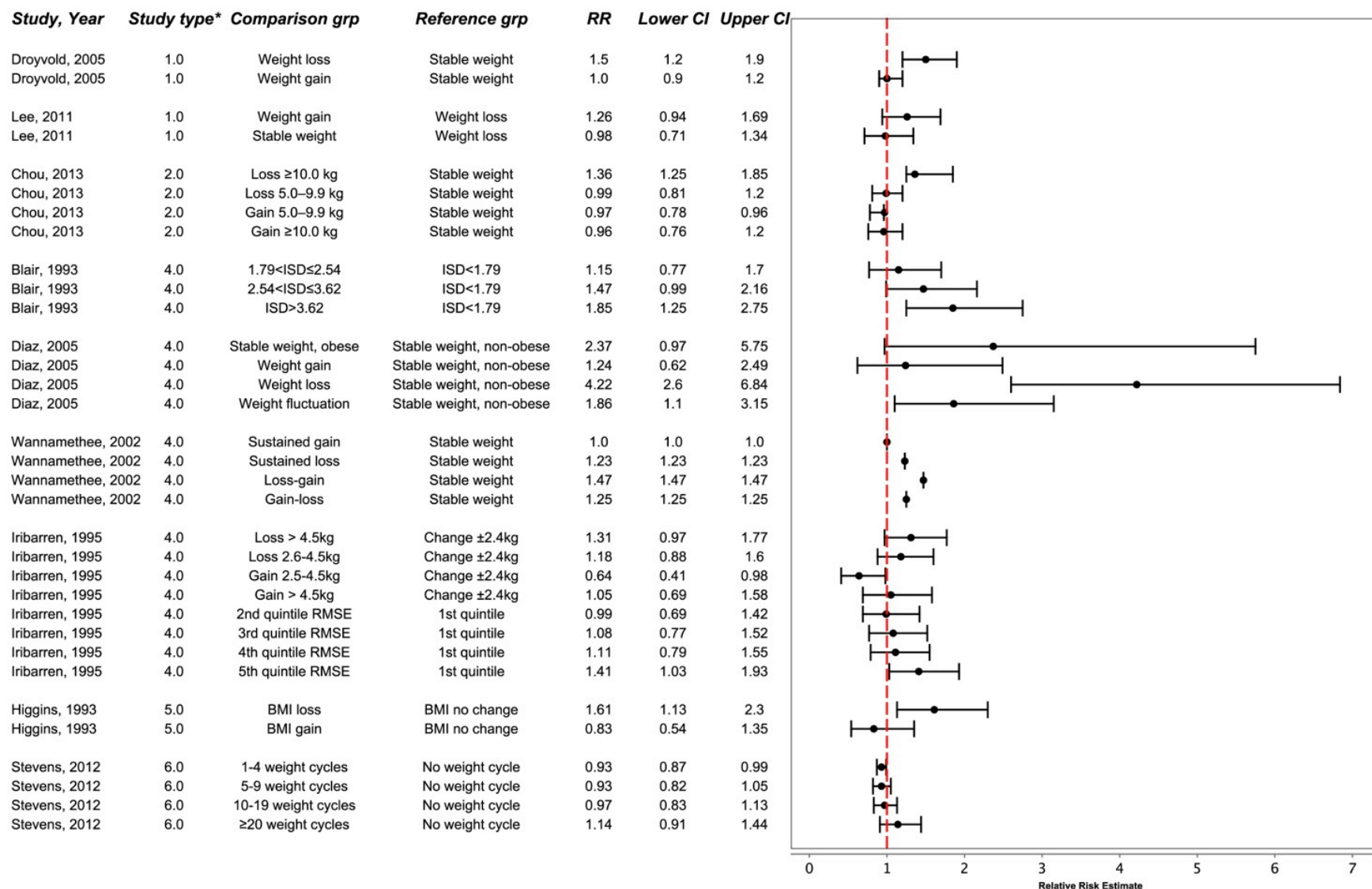
In the Dubbo Osteoporosis Epidemiology Study (AUS), while weight fluctuation increased risks of all-cause mortality in both men (RR=1.5, CI: 1.1–2.0) and women (RR=1.3, CI: 1.0–1.7), attributed risk due to weight variability was much lower (1.4–3.4%) compared with that for weight loss (11.6% in men and 10.9% in women) (16).

**Table 13 Forest plots comparing Included Studies with different study design types for the association between weight change with CVS mortality**



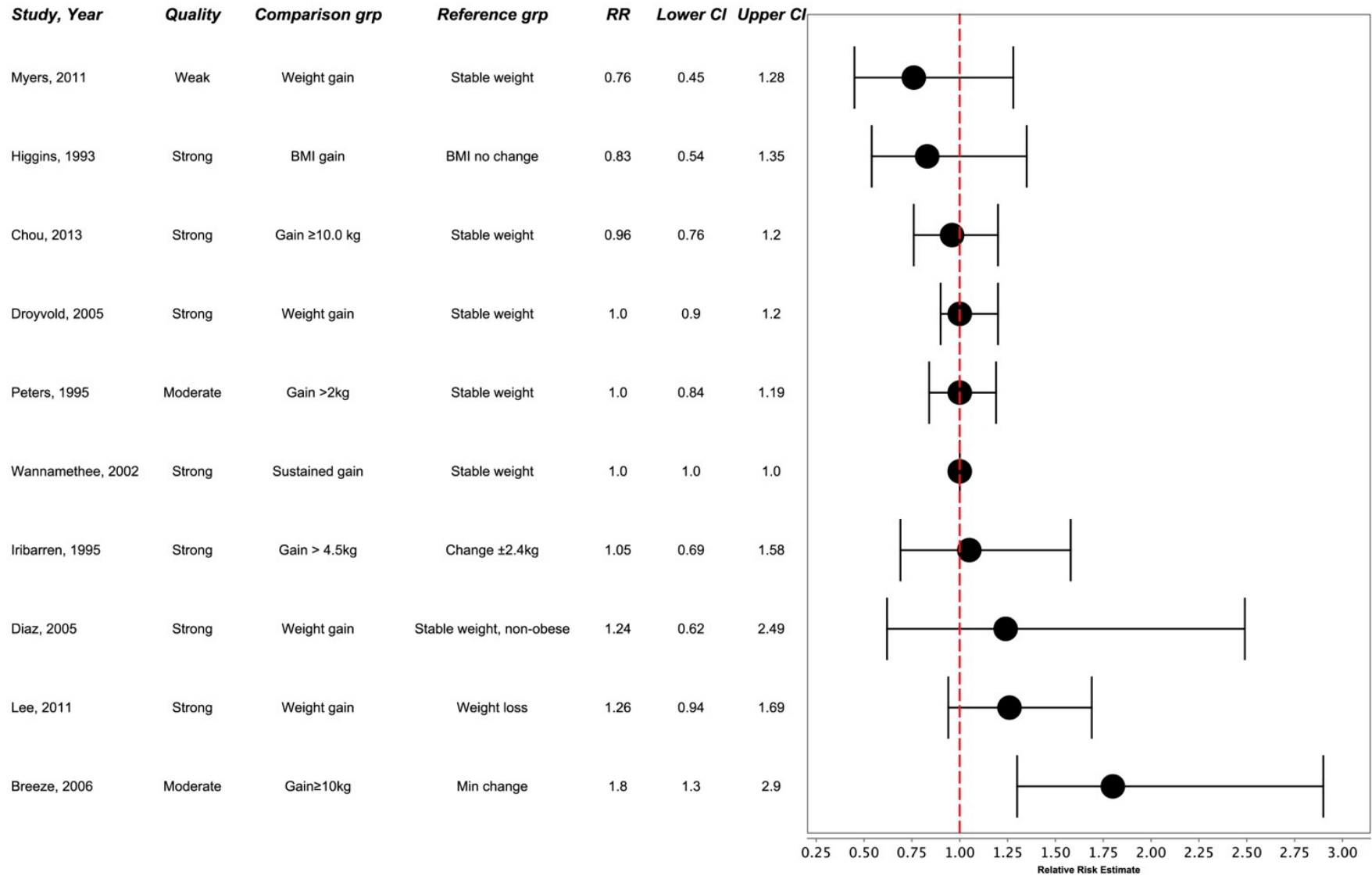


**Table 14 Forest plots comparing Included Studies with Strong EPHPP evidence rating for the association between weight change with CVS mortality**

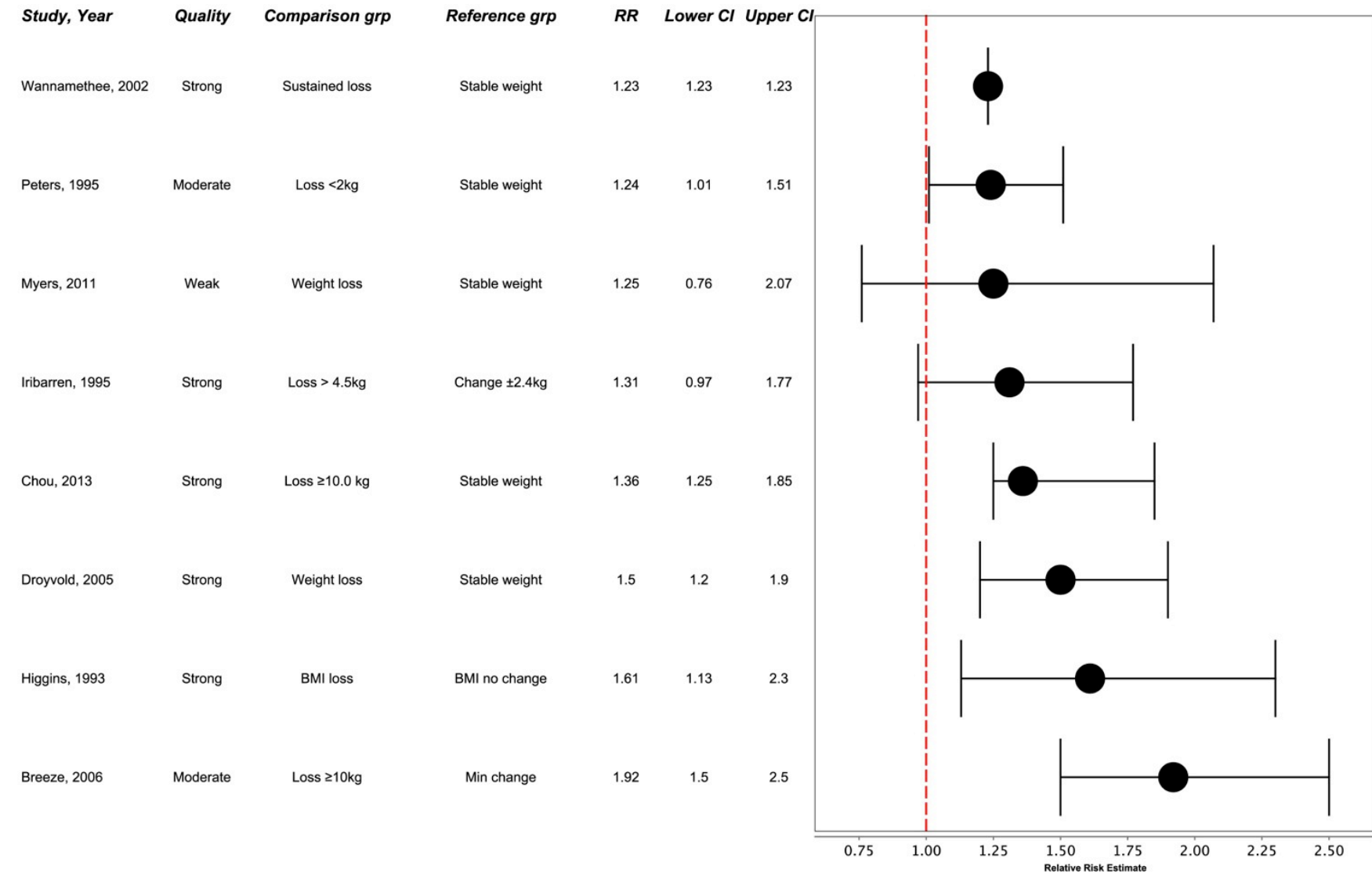




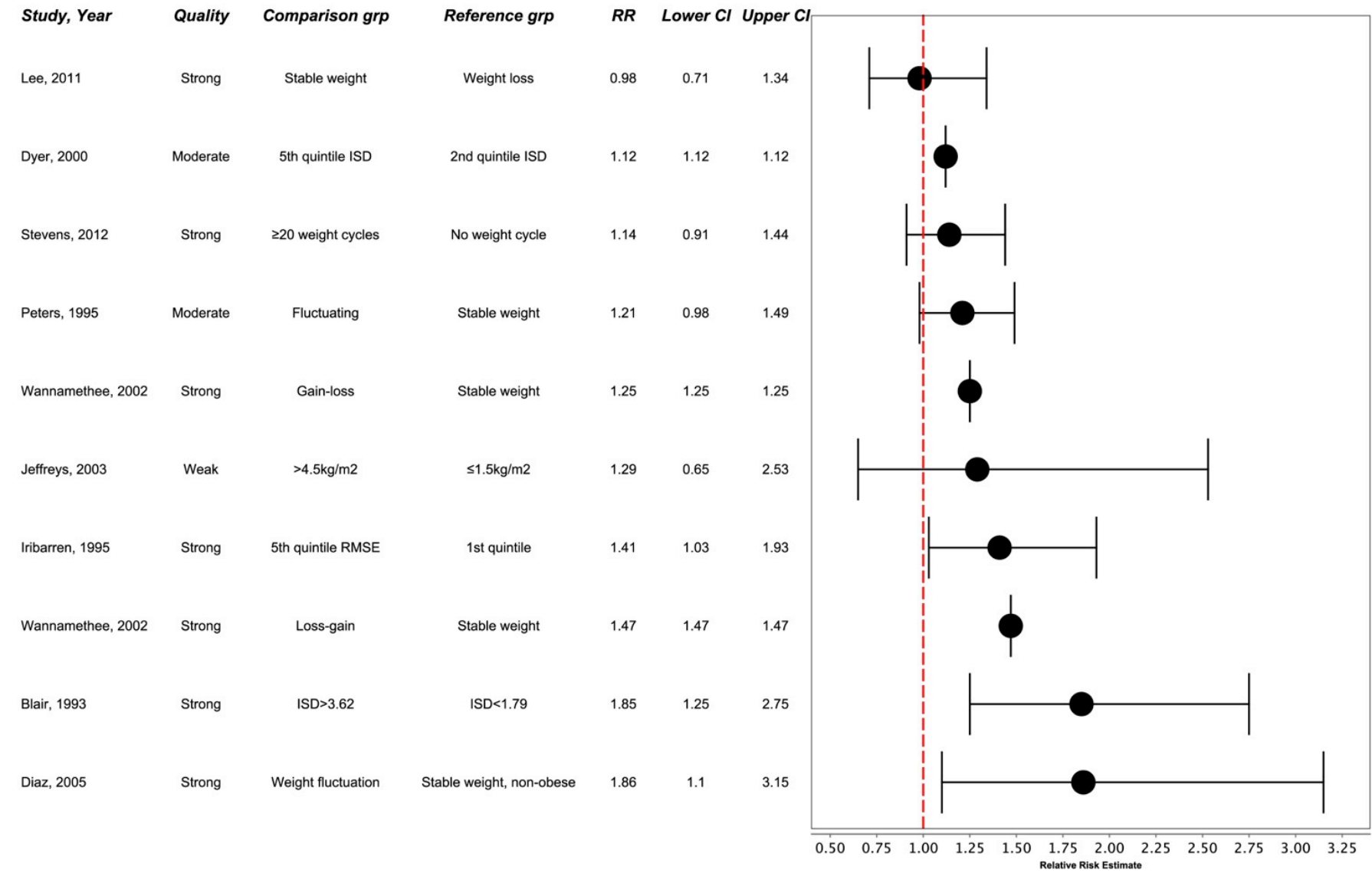
**Table 15 Forest plots comparing Included Studies on the relative risk association between subgroups of greatest weight gain versus reference group with CVS mortality**



**Table 16 Forest plots comparing Included Studies on the relative risk association between subgroups of greatest weight loss versus reference group with CVS mortality**



**Table 17 Forest plots comparing Included Studies on the relative risk association between subgroups of greatest weight fluctuation versus reference group with CVS mortality**



### 2.6.3 CHD mortality

Seven studies evaluated the impact of weight changes on CHD mortality (Table 18, Table 19, Table 20, Table 21 and Table 22) with the majority (four out of seven) assessing weight differences between two study examinations (study type 1) and one of them using recalled weight (study type 2).

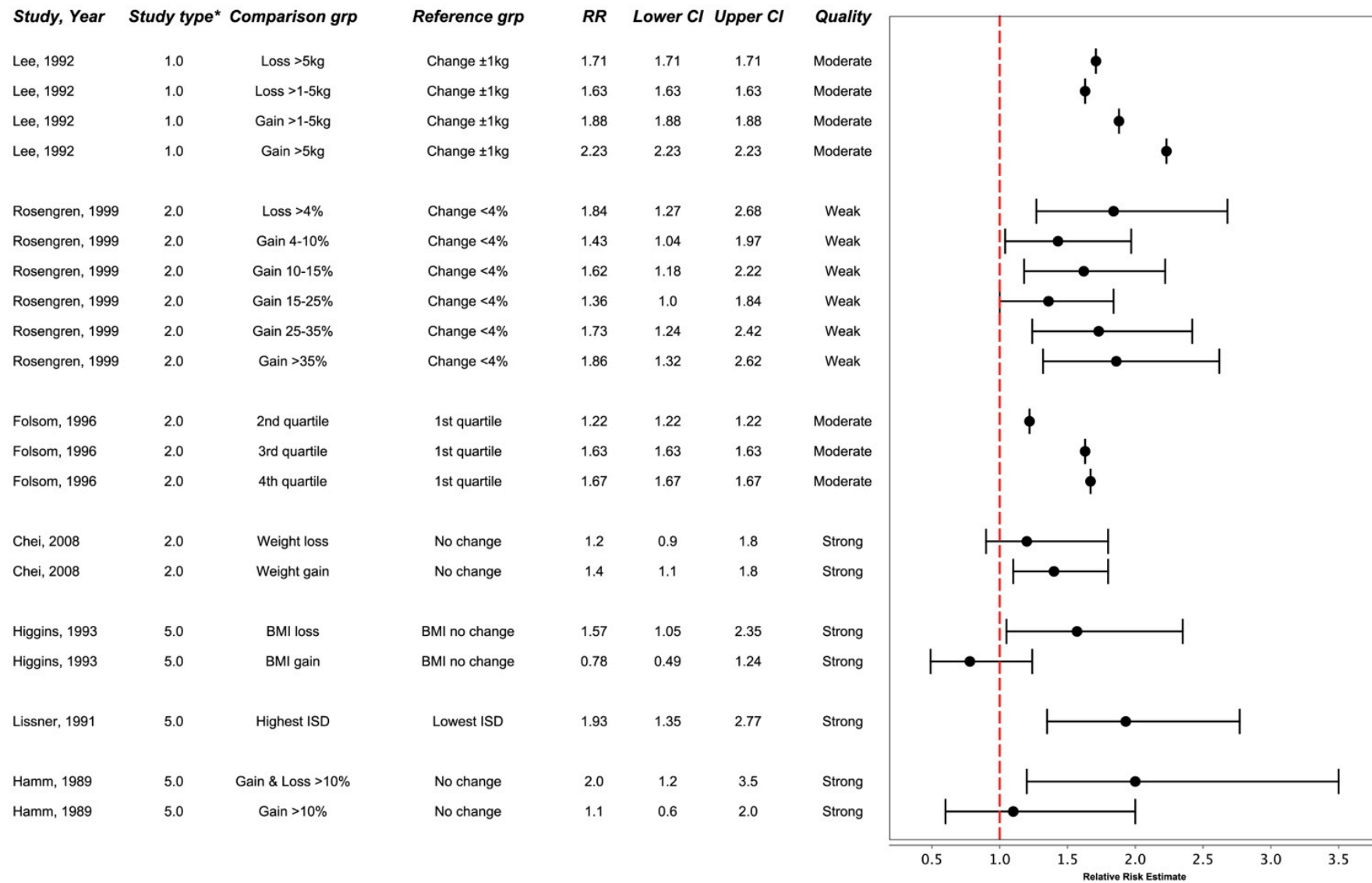
A “J-shaped” relationship was observed in the Harvard Alumni Health Study (33), where there was increased risk for CHD mortality for both men who experienced both weight loss of >5kg (RR=1.71, CI not reported) and those experiencing weight gain of >5kg (RR=2.23, CI not reported). Again, the findings for weight loss were unexpected and unfortunately data were not available as to whether weight loss was involuntary or intentional.

The control arm of the Multi-Factor Primary Prevention Trial (106) compared the difference between a recalled weight at age 20 to the first examination, and showed that increasing weight ( $p=0.004$  for trend), especially for men who gained more than 35%, resulted in higher relative risk of mortality from CHD (RR=2.76, CI: 1.97–3.85) versus men who remained weight stable ( $\pm 4\%$ ). Weight loss of >4% also was associated with increased risk of (RR=1.84, CI: 1.27–2.68). Similar linear trends were also reported in the Harvard Alumni Health Study (UK) (33) and the Iowa Women's Health study (US) (125).

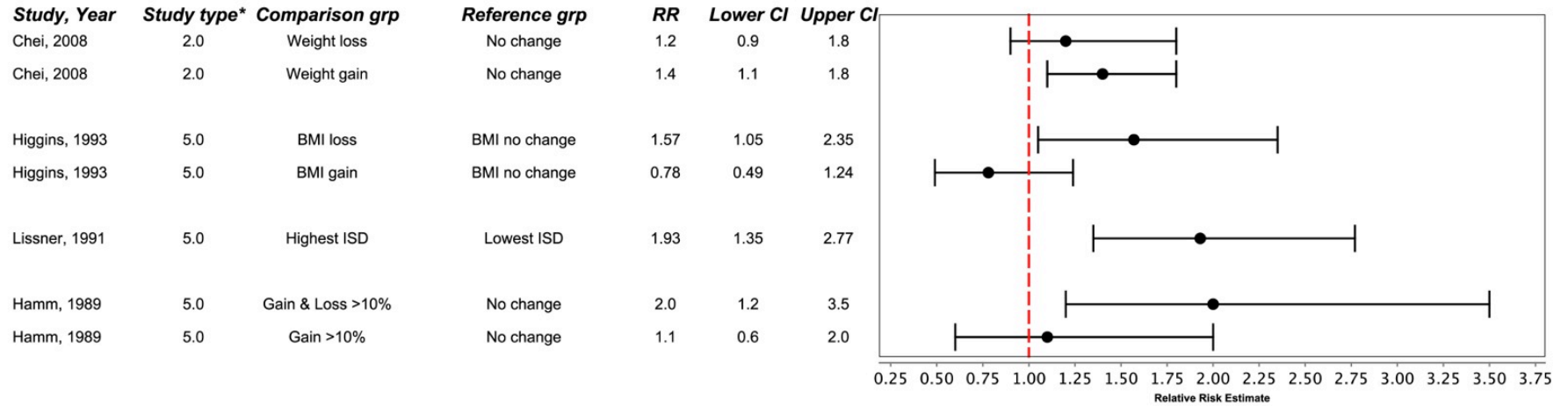
Results relating to CHD mortality for the Framingham Heart Study were similar to observations for all-cause mortality. BMI loss in middle-aged men and women conferred increased relative risks of (RR=1.57, CI: 1.05–2.35) while BMI gain was protective (RR=0.78,

CI: 0.49–1.24) for CHD mortality in later life (109). Men and women with highly variable body weights had increased all-cause and CHD mortality (RR=1.93, CI: 1.35–2.77) (17, 18). Both weight loss and gain were associated with higher CHD mortality risks in the Japan Public Health Center-based prospective study (JP) (122).

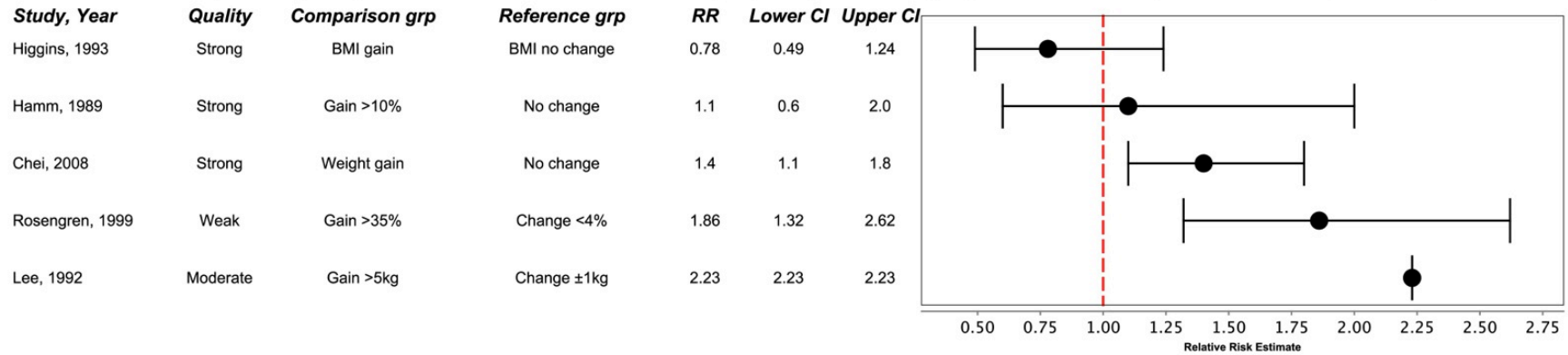
**Table 18 Forest plots comparing Included Studies with different study design types for the association between weight change with CHD mortality**



**Table 19 Forest plots comparing Included Studies with Strong EPHPP evidence rating for the association between weight change with CHD mortality**

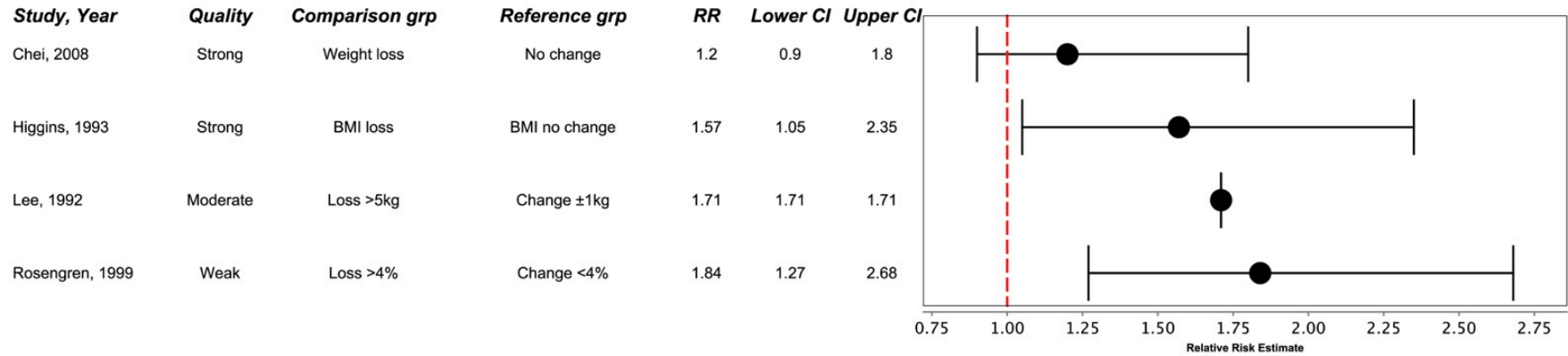


**Table 20 Forest plots comparing Included Studies on the relative risk association between subgroups of greatest weight gain versus reference group with CHD mortality**

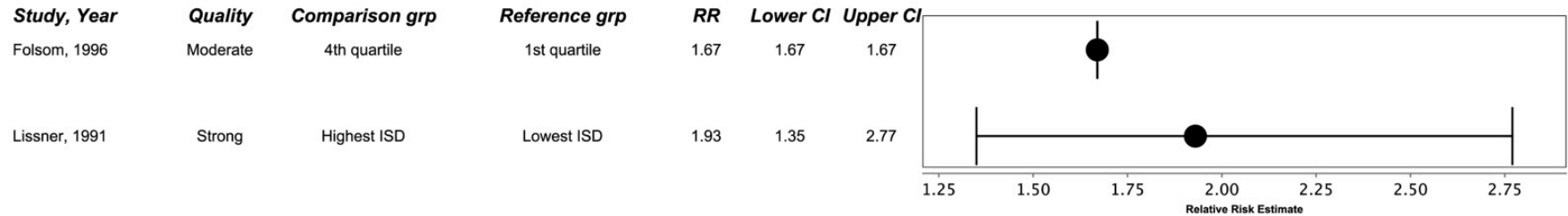




**Table 21 Forest plots comparing Included Studies on the relative risk association between subgroups of greatest weight loss versus reference group with CHD mortality**



**Table 22 Forest plots comparing Included Studies on the relative risk association between subgroups of greatest weight fluctuation versus reference groups with CHD mortality**



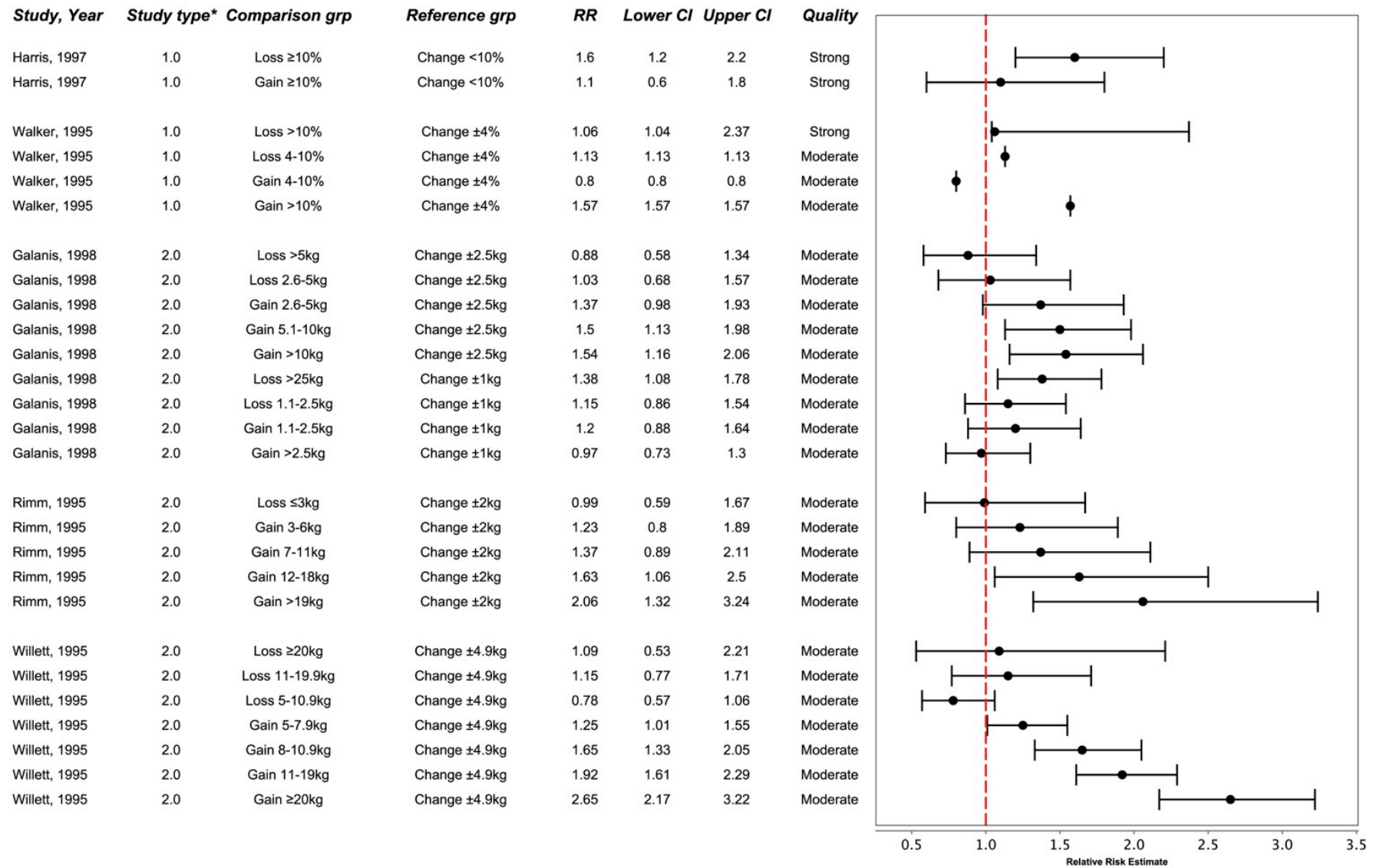
#### **2.6.4 First incidence of CHD**

Five studies evaluated the impact of weight changes on incidence of CHD (Table 23, Table 24, Table 25 and Table 26). Those studies that employed a study design of comparing differences between two examinations (study type 1) or between current weight and a recalled weight (study type 2) found a linear trend of increased risk of later life adverse outcomes with weight gain (124, 129, 130) and weight loss (120) in middle-aged adults.

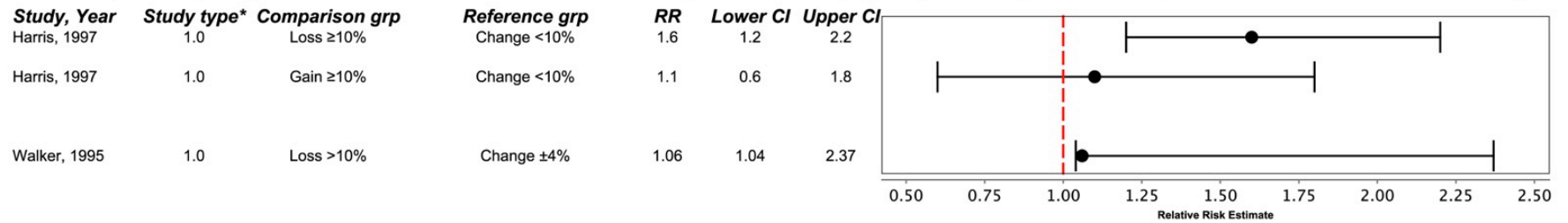
Findings from the Honolulu Heart Program (128) are unique in as they described risks of CHD incidence associated with early and late periods of weight change in the same individuals. Men who gained more than 2.5 kg between age 25 and examination 1 (1965-1968) had a significantly higher risk of incident CHD compared with men in the stable category (RR=1.37, CI: 0.98–1.93), and this excess risk increased progressively across the weight gain categories. Weight loss over this period was not significantly associated with CHD risk. For the period of later weight change, in contrast, risk of CHD increased progressively with weight loss. One plausible interpretation offered by the authors is that weight gain (adipose tissue) early in life led to the development of diabetes, which, in turn, was related both to later weight loss and increased risk of CHD.

The linear relationship between increasing weight gain and first incidence of CHD was also reported in the British Regional Heart Study (UK) (130), the Health Professionals Follow up Study (US) (129) and the Nurses' Health Study (US) (124).

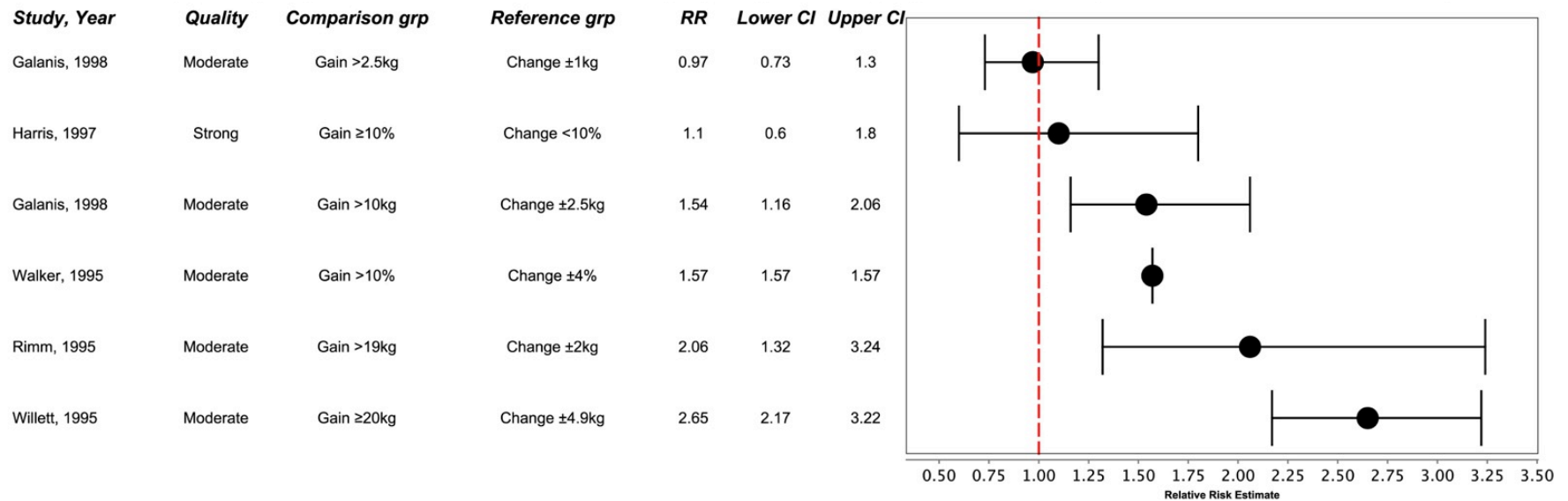
**Table 23 Forest plots comparing Included Studies with different study design types for the association between weight change with first incidence of CHD**



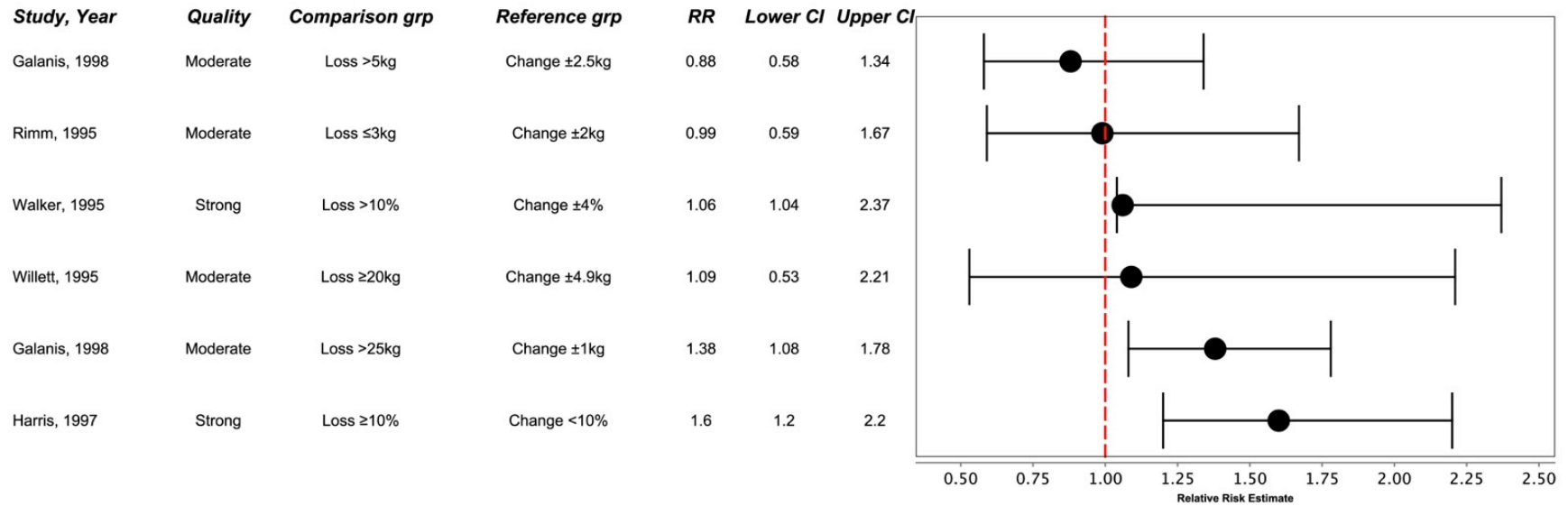
**Table 24 Forest plots comparing Included Studies with Strong EPHPP evidence rating for the association between weight change with first incidence of CHD**



**Table 25 Forest plots comparing Included Studies on the relative risk association between subgroups of greatest weight gain versus reference group with first incidence of CHD**



**Table 26 Forest plots comparing Included Studies on the relative risk association between subgroups of greatest weight loss versus reference group with first incidence of CHD**



## **2.7 Methodological issues**

### **2.7.1 Temporal separation**

Any attempt to understand associations between weight change or fluctuations and mortality or morbidity is particularly challenging and requires sufficiently long term follow up in order to permit exclusion of early deaths so as to disregard likely effects of illness-related weight loss. This is often referred to as a “temporal separation” between periods of weight change measurements and of follow up for outcomes. Several other factors such as time period over which weight change is measured, methods used to define weight change, period of life during which weight change is measured, classification of body mass index, confounding by smoking, intentional weight loss and pre-existing morbidities, all make interpretations and comparisons of results from various studies difficult. However, there is no strong evidence for the ideal number of years that would adequately account for illness-related weight loss, 15 out of 30 included studies used a temporal separation period ranging from 2 to 25 years (Table 2).

This effect was demonstrated most clearly in the study conducted among Harvard University Alumni (33), where U-shaped relations between weight change and mortality from all causes and from CHD but not from cancer were observed for deaths within first 5 years, but when limited to only deaths after the 5th year of follow up, lower relative risks were observed. Although it was considered that studies with temporal separation would be more robust, one study reported minimal effects after adjusting for it. In the Chicago Western Electric Company study (107), weight variability was significantly related to CVS mortality for both years 1-15 and years 16-25, with little or no difference in relative risks being seen for the two follow up periods.

### **2.7.2 Studies with measurements at only two-time points**

There are also problems with statistical methods or research designs, especially in studies that only employed two time points (18 out of 30 included studies). Change in weight/BMI between two time points is not ideal for studying development because the collection of individual trajectories is limited to a collection of straight lines. While two observations of BMI or equivalent measures such as waist circumference or waist-hip ratio provide information about the amount of change, they address other research questions quite poorly, such as the investigation of drivers of both average change in BMI and individual variability in change in amplitude and frequency. How may one infer genuine causality between an early life exposure and later health? The use of standard multivariable regression models to determine the association of weight/BMI change on a later life outcome (all-cause mortality, first incidence of CHD, CVS or CHD mortality in this review) can be challenging to interpret due to conditioning of the weight change exposure variable and distal mortality outcome (138).

### **2.7.3 Weight fluctuation**

12 out of 30 included studies (study type 4, 5 and 6) established a form of weight fluctuation or variability variable over multiple time point measurement of weight or BMI. One key aspect in comparing these weight variability studies is the method used to quantify weight fluctuation. It is commonly understood that there are two main measures: the coefficient of variation (CV) and the residual mean square error (RMSE) methods. However even with the former, there are at least three different ways of calculating the CV:

1. The coefficient of variation (CV) that is calculated as the standard deviation of each individual's body mass index values at each assessment divided by the mean body mass

index for that individual (13, 16, 17, 62, 109). This value reflects the extent to which an individual's body mass index fluctuated around his or her own mean value.

2. The coefficient of variation (CV) that is calculated as the standard deviation of each individual's body mass index values at each assessment divided by the mean body mass index for the entire cohort under study (12). This value reflects the extent to which an individual's body mass index fluctuated around the population's mean value.
3. The coefficient of variation (CV), calculated as the standard deviation of BMI and the standard deviation about the individual's BMI regression (107). This value reflects the extent of each individual variation about the trend in BMI over a time period or the mean of his/her BMI regression/trend over time and aims to remove from the measure of weight variability that portion of variability due to systematic gain or loss in weight.

The residual root mean square error (RMSE) (adjusted for the average and the linear slope of weight) method captures the component of variation in weight that is inconsistent or not linear that is independent of the level and trend, and is obtained from the linear regression model of each individual over the study period (135). Therefore, it has been argued that the RMSE is a more sensitive index of weight variation than the CV, which is correlated with the linear slope of weight.

Other methods employed to derive a measure of fluctuation or variation include summing absolute deviations between initial and final BMI values, as used in the Erfort Male Cohort Study (DE) (14) where the extent of weight fluctuations were ascribed to those respondents,



whose initial and final BMI differed by  $<3 \text{ kg/m}^2$  and whose sum of absolute deviations were  $>3.49$  BMI-units.

Another approach was taken in the British Regional Heart Study (UK) (15), where men were divided into groups based on their weight change from baseline, 2<sup>nd</sup> and 3<sup>rd</sup> assessment. Weight fluctuation was defined as weight loss from 1<sup>st</sup> to 2<sup>nd</sup> assessment followed by weight loss from 2<sup>nd</sup> to 3<sup>rd</sup> assessment or weight gain from 1<sup>st</sup> to 2<sup>nd</sup> assessment followed by weight loss from 2<sup>nd</sup> to 3<sup>rd</sup> assessment.

Finally, in the Western Electric Study (US) (18), where each participant's self-reported weights at ages 20, 25, 30, 35, and 40 years were used to calculate percentage change in weight from ages 20 to 25, 25 to 30, 30 to 35, and 35 to 40. The maximum percentage gain and the maximum percentage loss were identified in each participant's series of four percentage changes. Men were included in the gain and loss group when the maximum gain during any one five-year period and the maximum loss during another five-year period were each 10 per cent or greater. These groups were compared with the no-change group, which comprised men whose largest gain and largest loss were each less than 5 per cent and whose weight at initial examination differed by less than 5 per cent from the reported weight at age 20.

#### **2.7.4 Cox's proportional model**

All 30 included studies grouped subjects into weight change categories based on their absolute or relative differences in measurements of weight/BMI at two time points or trend of weight change over multiple time points, and employed Cox proportional hazards regression

models (139) to calculate age-adjusted and multivariable adjusted mortality hazard ratios associated with each group (weight loss, gain, fluctuating), mostly using the weight stable group as reference.

However, as Cox's models do not estimate the baseline hazard (mortality) function, one can make only comparative, not absolute, statements about the hazard. Therefore, in interpreting the findings of these studies, one can say that the hazard for one group is three times that of another but we cannot say how high or low the absolute effect of the exposure is (in this case, weight change) (140). Another shortcoming of the use of standard Cox's models is that, the assumption of proportionality is made; that is, the hazards of two subjects with different exposure status are assumed to be proportional with the same proportionality factor at all ages in the follow-up period (141). This may be a considerable limitation as different life stages such as post-natal, childhood, adolescent, adulthood and post-menopausal are likely to exert different effects on the individual's weight change and outcome, especially if the follow-up period extends over several decades within these studies.

## **2.8 Discussion**

Methodologically, there are three main conditions that need to be met in order to infer a "causal effect" between weight change and mortality. Firstly, the presumed cause and effect must be assumed to be related. Secondly, the presumed cause must precede the effect in time and thirdly, other competing explanations (confounding factors) need to be ruled out (67). Thus, it is only with longitudinal cohort weight change studies that researchers are able to make causal inferences with prospective data in which the outcome of interest in later life is the result of the

entire pattern of weight change in individuals across the life course. It is important to note that when change in body size with age is linked to a later adverse outcome, it is the change in size across the whole time interval between the measurements, not just in early life, that is implicated (11).

However, isolating the differential effects of weight change, fluctuation or variability, onset, persistence or duration of obesity in this review is challenging, as these research objectives were often not among the original goals of established longitudinal prospective cohorts, which were mostly concerned with cardiovascular disease, diabetes and cancer. Nevertheless, this review retrieved a total of 30 prospective studies with all-cause mortality and CVS/CHD mortality outcomes that met the selection criteria.

Overall, the relative risk of weight gain on all-cause mortality can be challenging to interpret as both significant protective and non-protective effects have been identified in 16 studies. Ten of these reported increased risks of all-cause mortality resulting from large weight gain, with increases of 2% to 40%. Three studies (108-110) reported protective effects of 11% to 36% while three studies demonstrated little differences between those who gain the most weight versus having a stable weight. Interpretation is further complicated by the lack of standardised weight categories even when simply comparing hazard ratios for those with greatest weight gain (Table 9). Findings comparing hazard ratios of greatest weight loss groups were more consistent as all studies reported an increased relative risk of 21% to 88% (Table 10). Similarly, high weight fluctuation is associated with significantly increased risk in all-cause mortality except in three studies that reported minimal effects (Table 11).

Of the three studies that reported protective effects of weight gain on all-cause mortality, two did not employ any temporal separation (108, 109); one adjusted for physical activity (108) but not smoking. On the other hand, a large prospective study (n=75,868) reported protective effects of weight gain but this might reflect the unique rural India context, in which low BMI itself has been considered as a marker of under-nutrition, poor hygienic conditions, low SES and little access to medical care. As such, its findings may not be directly generalizable (110).

The literature supporting the hypothesis that increased mortality risks from weight changes are actually determined to a large extent by unfavourable lifestyle factors, pre-existing diseases or cardiorespiratory fitness, are limited but compelling. In particular, evidence from the Aerobics Center Longitudinal Study (US) found that men who lost fitness had a higher mortality risk regardless of BMI change compared with the reference group, men who improved fitness and decreased BMI. At the same time, men who improved fitness were more likely to attenuate the negative effects of BMI increase on all-cause and CVS mortality (112). As this is the only included study that considered fitness change, it is difficult to assess whether weight/BMI change in other studies was associated with mortality independent of fitness change.

Similar patterns (Table 15, Table 16 and Table 17) were observed for the included studies with CVS mortality as an outcome with ten out of 13 included studies that investigated both CVS and all-cause mortality consistently reporting lower hazard ratios for the latter outcome (12, 34, 35, 62, 107-109, 112, 121, 135) and with only three studies reporting negligible differences observed (13, 15, 133).

Seven of the included studies had CHD mortality as outcomes including four with a strong EPHPP rating for methodological quality (Table 19). These four studies provided similar evidence for significant increased risk of about 90% for both men and women with highest weight fluctuation. However, results for risks due to weight gain were mixed across studies. A significant increase in risk (RR=1.4, CI: 1.1–1.8) was reported in the Japan Public Health Center-based prospective study (JP) of over 80,000 (men and women); a protected effect (RR=0.78, CI: 0.49–1.24) was reported in the 2,500 (men and women) from the Framingham Study (US); no comparative increase/decrease in risk (RR=1.1, CI: 0.6–2.0) was reported with weight gain in 1,959 men from the Western Electric Study (US).

Positive linear trends of increasing hazard ratios were consistently observed in four out of five included studies with first incidence of CHD as a later life outcome (Table 23). Within each study, the lowest risks were conferred to categories of lowest weight loss and the highest risks to categories of greatest weight gain. None of these studies investigated effects of weight fluctuation. When comparing only subgroups of greatest weight gain and loss across all five studies, the effect of the former was more pronounced than for latter.

Therefore, findings from this review suggest that, when compared to maintaining a stable weight during adulthood:

- Large weight gain and loss between two time points results in marginal to significant increases in risk of first incidence of CHD and all-cause, CVS and CHD mortality in later life, depending on presence of lifestyle and latent morbidity factors (moderate evidence)

- Large weight fluctuation across multiple time points increases risks of all-cause, CVS and CHD mortality in later life (strong evidence)

There is a need for caution in interpreting the apparent increased hazard ratios observed for weight loss, as it remains unclear whether weight loss *per se* is causally related to increased mortality. With Cox's regression models, it is not possible to separate completely the effects of early and late changes in weight given the proportional hazards assumption. Thus, the excess risk associated with weight loss may be related to residual confounding of weight and weight gain earlier in life or pre-existing cardiovascular disease or diabetes and the adverse health effects of smoking (14), or to a history of some other morbidity that the studies were not able to adequately measure. This is especially so since underlying reasons for weight losses were not determined in these studies. This reasoning is reinforced by a meta-analysis (113) with a focus on intentionality of weight loss among unhealthy subjects (excluded in this review) which found that weight loss appeared to benefit unhealthy obese weight losers (RR=0.84, CI: 0.73–9.97) but had no benefit for healthy obese and overall, there was no change in risk for the obese groups (RR=0.94, CI: 0.86–1.04). In particular, weight change over a relatively short period of time, e.g., between two examinations, was more likely to be influenced by illness-related weight loss than is weight change since young adulthood (128). Pinpointing the critical period of weight change was also not addressed in any of the studies in this review.

There is however, strong biological reasoning supporting an increased relative risk from weight fluctuation. Thermogenesis studies utilising animal and human models have put forward evidence suggesting that the process of “catch-up growth” or recovering body weight itself

(especially in the context of weight fluctuation or cycling) is an independent risk factor for the development of cardiovascular disease and consequent increased susceptibilities to chronic metabolic mortality (142).

Other issues that remain important for future reviews include investigation of: the mechanism by which social-economic status (SES) in early life influences obesity in adulthood (49); whether the relationships between birth weight and maturation and later obesity persist after accounting for confounding factors; whether any relationships between dietary factors and activity and excess weight in later life are due to a direct effect, or to tracking in dietary or activity behaviour (55, 61); how psychological factors and behaviours influence energy balance, and therefore degree of obesity (48); and the impact of the duration of obesity on the risk of mortality (50, 51).

## **2.9 Conclusions**

In summary, the currently available evidence suggests that excessive weight gain and fluctuation increases marginal to significant risks of death depending on the presence of lifestyle and latent morbidity factors. Therefore, it is reasonable to place more emphasis on the importance for adults of maintaining stable weight at a desirable level throughout mid life. At the same time, the reader should also appreciate the reality that much of the outcomes of published studies trying to model the effects of weight change or differences between two time points on a later life outcome were not directly comparable due to the lack of a standardised weight change unit scale and the inherent conditioning of the weight change term or other explanatory variable terms from using standard multivariable regression techniques (which can result in both positive

and negative regression coefficients, thus rendering any hypothesis of the effect of weight change on the outcome non-plausible in statistical terms) (11, 138).

More broadly, there is a lack of basic information on the normal degree of weight changes and fluctuation patterns in a healthy population over the human life span, which would be extremely helpful in itself as a baseline to compare significant deviation from the norm in exerting independent direct or indirect effects on a later life outcome.

More recent analytical techniques such as duration of obesity models (126), dynamic path analysis (141) and latent class growth models (73) may provide further insights and methods to help researchers better describe and compare weight changes over time within a life span (143) so as to understand mechanisms that underlie the aetiology of chronic diseases. Past and on-going longitudinal cohort studies in Singapore have not yet been sufficiently exploited. More research in adolescent growth patterns is required.



## Chapter 3: Data sources and preparation

### Synopsis

Of the 30 Included Studies in the systematic review in Chapter Two, none had a study period that included the effects of weight changes during childhood and/or adolescence with only a few studies requesting subjects to recall weight at age 18 (124) or 20 (106) at the most. It seemed that the majority of studies investigating early life growth measures have focussed on its association with growth attainment, for example BMI or skin fold thickness in later childhood or obesity in adulthood. Any associations found between early growth may also inherently be less useful considering that adult BMI, in itself, mediates the interaction between early growth patterns and subsequent disease risk (22) and thus, it is reasonable to conclude that only with longitudinal cohort weight change studies that researchers could attempt to make causal inferences using prospective data in which the outcome of interest in later life is the result of the entire pattern of weight change in individuals across the life course.

Given the paucity of longitudinal anthropometric data sets in Singapore, I conceived the idea of establishing a new longitudinal cohort that could provide repeated anthropometric measurements of children and adolescents annually from ages 7 to 16. This would be achieved by record linkage of two large school-based health-screening programmes.

Therefore, in this Chapter, I explore the feasibility of, and methods of data preparation needed to merge two routine school health screening data to establish a new longitudinal data set for subsequent analyses of the anthropometric development of youth in Singapore. At the same

time, separate sub-datasets were prepared for use in Chapter Five, Six and Seven, with their details presented in each respective chapter.

### **3.1 Introduction**

#### **3.1.1 Brief history of Singapore's School Health Service**

The origins of Singapore's School Health Service (SHS) can be traced back to the early 1920s – much before the beginnings of the current Health Promotion Board (HPB). At that time, common health problems faced by school children included measles and typhoid; dental caries; anaemia among girls; visual defects and malnutrition. In response, the Singapore administration initiated a programme comprising two part-time doctors who covered about 5,000 school children in the seven schools of Singapore. School visits did not include standardised services and referrals; rather health problems identified were treated on the spot at the school premises (92).

Economic hardship during World War II and the immediate post-war period saw an overall deterioration in the health of the school-age child. There was an increase in malnutrition (including anaemia due to worm infestation and malaria), a high prevalence of tuberculosis, and recorded outbreaks of poliomyelitis, diphtheria, and small pox (92). However, following independence after 1965 and the subsequent economic growth and urbanisation in Singapore, the health status of school children significantly improved with the expansion of the immunisation program (including introducing poliomyelitis immunisation in 1964, and measles vaccination in 1997) and routine school health screening (including growth monitoring and backbone screening for scoliosis) (144)

In 2001, when the MOH's departments on National Health Education, Nutrition, School Health Service, School Dental Service and its Health Promotion Division were amalgamated, the implementation of the SHS was taken over by the HPB, which currently reaches out to around half a million primary and secondary school children nation-wide. The services provided have essentially remained the same, but for a few changes to the educational stage at which children are screened and immunised.

As of 2011, 10 primary and 12 secondary school health teams, supervised by 12 nurse managers have delivered the services. Each primary team comprised eight to nine nurses, and a medical officer. Each secondary team comprised three to four nurses. The primary and secondary school health teams were divided between four geographical zones of the SHS programme, namely, north, south, east and west.

Data on the SHS are captured using a web-based data entry system called School-based Health Programme System (SHPS), which had been implemented since 2001. New data from each health screening is uploaded from the school teams to the central server at the HPB and school health teams are also able to access the data in real-time.

The HPB's Student Health Centre (SHC) provides clinic-based preventive and screening services for students, and it also serves as a referral centre for the SHS. Students referred with suspected abnormalities, such as those relating to growth and development (short or tall stature and pubertal development delays), and vision, hearing, scoliosis and heart conditions, are re-examined and managed at the Centre's clinics.

## **3.2 Health Promotion Board**

### **3.2.1 Youth Health Division**

The Youth Health Division (YHD) comes under the purview of a Statutory Board, the Health Promotion Board (HPB), which was formed in April 2001. There are seven Divisions in HPB (as of August 2013):

- Adult Health Division
- Healthy Ageing Division
- Youth Health Division
- Research & Strategic Planning Division
- Corporate Services Division
- Corporate Marketing & Communications Division, and
- Community Partnership

The mission of Youth Health Division is to promote good health and reduce illness among the school-age population in Singapore. There are three main subdivisions in YHD; Programme Development, Programme Outreach & Preventive Health Services. The departments under Preventive Health Services are:

- School Health Service
- Student Health Centre
- School Dental Service, and
- Clinical Standards & Quality Department

The main functions of YHD for the school-age population are to ensure early detection and management of health problems through health screening in schools; prevention of communicable diseases through immunisation; improvement of health status through health promotion; prevention of dental diseases through early detection, fissure sealants and regular maintenance and oral health education; the provision of basic dental treatment like scaling, polishing, restorative work and extraction; conduct school-based and the provision of clinic-based screening and immunisation services.

The School Health Service (SHS) department is responsible for the school-based health screening and immunisation programme. The two main objectives of the department are to detect common health conditions among the school-going population through screening and to prevent illness from communicable diseases through immunisation.

Annually, there are about 500,000 students enrolled in 203 primary schools and 172 secondary schools and the department's measurable targets for the year are to screen at least 95% of Primary One and Primary Five pupils and to achieve 95% of immunisation coverage.

### **3.2.2 Health screening in primary schools**

Screening in primary schools includes a height and weight check for Primary One and Primary Five students followed by a medical examination, which also serves to assess them for fitness for immunisation. In Primary One, the medical check by the doctor includes a nutritional status assessment (height for age, weight for age, and weight for height), audiometry test (for hearing problem) and vision screening (including stereopsis test). In Primary Five the medical

examination also includes nutrition status assessment, vision screening (including colour vision assessment) and pubertal assessment. New entrants to the school also receive the medical examination. The school health teams review students from other levels identified with health problems in previous years. Previously Primary Six students were screened instead of Primary Five. Due to changes in national childhood immunisation from Primary Six to Five in 2008, the screening grade was also changed. Only in 2008, both Primary Five and Six students received the medical examination.

All students from Primary Two to Four and Six are also interviewed to assess general health. Vision screening for visual acuity is done at all levels in primary schools using Snellen's test method. In a few schools, Logmar testing is conducted. Group audiometric tests (of 10 children each) are done for Primary One students. Forward bending test (FBT) for girls in Primary Five (during medical examination) and Primary Six (during health interview) is done to screen for abnormal angles of trunk rotation as a preliminary test for scoliosis.

Four weeks before the health team visits the school, letters and information booklets about SHS and the health screening are given to the schools to distribute to parents. Even before the school academic year starts, during the orientation day (usually in Nov/Dec) for parents of children enrolled for Primary One the following year, a booklet "Information for Parents" providing information on youth health services is also distributed to parents.

During health examination, pupils who are identified with health conditions will either be referred to Student Health Centre for further assessment or followed up in school depending on

the needs. The most common health conditions include heart murmurs, short or tall stature, scoliosis, vision and hearing defects.

Students who require further assessment are referred to the Student Health Centre (SHC) e.g. students who are too tall for their age (height-for-age above the 97th percentile), too short for age (height-for-age below the 3rd percentile) or if there is evidence of a hearing loss of 30 decibels at two or more frequencies is detected; if heart murmurs are detected during medical examination; and if non-descended testes are identified. Primary Five, Six and Secondary One girls and all Secondary Two students with an angle of trunk rotation of 5 degrees or more are also referred to the SHC. Students already being assessed by their general practitioners are not referred to the SHC.

All Primary One students with visual acuity of 6/12 or more (tested on a Snellen's chart) are referred to the HPB's refraction clinics (managed by the National Myopia Prevention Programme). Students with visual problems in Primary Two and above are referred to their optometrist.

### **3.2.3 Health screening in secondary schools**

In the secondary schools, the nurses provide vision screening for secondary 1, 2 & 4 students. All students with existing health conditions are reviewed. In secondary 1, the girls are screened for scoliosis and in secondary 2, both the boys & girls are screened for scoliosis. In addition, secondary 2 students are assessed on the pubertal stage and also asked about their smoking behaviour.

### **3.2.4 School-based immunisation**

Immunisations are given as per the National Childhood Immunisation Schedule. Measles and diphtheria vaccinations are mandatory under the Infectious Disease Act (1976). All Primary One students receive a booster dose of the combined MMR vaccine against measles, mumps and rubella, and a second booster of oral polio vaccine against poliomyelitis. Primary Five students receive a second booster against diphtheria, tetanus and a third booster against poliomyelitis. Those who missed their immunisation in schools for whatever reasons such as incomplete consent form or unwell are referred to the SHC. Health teams also follow up on students from other levels who do not completed their immunisations as per the schedule.

### **3.2.5 Computerised data management system**

The School-based health screening programme system (SHPS), is a wireless web-based computer system implemented in 2000. It was upgraded in 2012 (SHIP) to real time online direct access to SHAPE, the main repository computer system. It allows direct data entry and viewing of information by multiple users within the school and displays medical data of the student from previous screening episodes in school as well as in Student Health Centre. Referral letters are printed in schools immediately following the direct on-site upload and download of referral data from SHAPE, for appointment scheduling via direct online access. Health assessment summary records are also printed in the school and given to the students for their parents' information and retention.



### **3.2.6 School Health Centre**

School children who are identified during the field health screening to have health problems are referred to the Student Health Centre (SHC) for further evaluation and management. Immunisations are provided under a comprehensive National Childhood Immunisation Schedule in Singapore.

The Student Health Centre serves as a referral centre at a primary care level providing preventive and screening services for school children and preschool children referred by the field screening teams in School Health Service and National Myopia Prevention Programme. It comprises general and specialist clinics, nutrition clinic, immunisation clinic and refraction clinic. Attendance at SHC is by appointment. The health problems referred tend to be related to growth and development problems (such as short and tall statures, underweight, overweight and pubertal problems), defective vision, hearing loss, scoliosis, heart condition detected at screening (such as heart murmurs) and other health problems detected during screening in schools. School children requiring further specialist assessment could be referred to the appropriate SHC specialist clinics (Cardiac Clinic and Endocrine Clinic) or the specialist clinics in the restructured hospitals.

Under MOE's Holistic Health Programme, students from primary 1 to junior college 2 who are overweight (BMI for age Percentile  $\geq 97\%$ ) or severely underweight ( $< 3\%$ ) are referred to the SHC.

At the SHC, these students are screened to exclude any medical conditions (e.g. endocrine disorders associated with excessive weight; eating disorders associated with underweight) and provided with lifestyle counselling to modify their dietary and physical activity habits. For the overweight students, their fitness to engage in Physical Education lessons in school is also assessed.

Blood tests such as fasting blood sugar (to exclude diabetes) and Lipid profile (to exclude abnormalities of lipids in the blood) are ordered. The thyroid function test is administered when indications (e.g. short and obese students) arise. Students who present with medical conditions or abnormal blood test results are subsequently referred to visiting specialists (e.g. endocrine Clinic in the SHC) for further follow-up and management. SHC also sees pregnant girls under 16 years old for mandatory pre-abortion counselling. A certificate of attendance is issued following, which the girls return to their gynaecologists.

### **3.3 Ministry of Education**

#### **3.3.1 Trim and Fit**

In 1992 Singapore's health ministry launched a "Trim and Fit" (TAF) national programme promoting a healthy lifestyle to address the common risk factors for chronic diseases such as obesity, physical inactivity, and cigarette smoking. Different age groups in the population were targeted, including school children. The health promotion board of the health ministry works in close partnership with the Ministry of Education (MOE) on obesity programmes for school children. The TAF programme for primary, secondary, and pre-university schools aimed to reduce obesity in school children and improve the physical fitness of

the pupils using a multi-disciplinary approach targeting overweight students, parents, teachers, and the school environment. Under the programme, nutrition education was integrated into the formal school curriculum. The food and drinks sold in school canteens were subject to control measures, and water coolers were provided in all schools to encourage students to drink more plain water. Schools that achieved good health outcomes were presented with the “Trim and Fit” awards annually.

As an incentive to schools for participating in TAF, the MOE presented TAF awards annually to schools in recognition of their efforts in improving physical fitness and reducing obesity in their schools. Each year, schools were banded according to their fitness index, results in the National Physical Fitness Award (NAPFA) test and percentage of overweight students.

On the other hand, the concept of TAF program had also been criticised for its lack of interesting activities and the potential stigma involved with being part of a “fat” club (145). Not surprisingly, the TAF programme was replaced in 2008 with the Holistic Health Framework (HHF), which looked at a student's physical, mental and social health. The new program was meant for all students, not simply for those who were overweight, and aimed to generate more interest in a healthy lifestyle among them. Also, schools had the autonomy to implement their own programmes to achieve these objectives, instead of following a regimented set of physical activities. With the new HHF in place, many schools took different approaches such as including the underweight students in the club, so that they could reduce the obesity stigma associated with the previous TAF Club and focusing their activities on encouraging students to play sports and games.

### 3.3.2 Holistic Health Framework

The Holistic Health Framework (HHF) was launched in May 2006. This was a framework that allowed schools to bring together in a purposeful manner the key areas, programmes and processes that develop the physical, mental and social health of their students (146). The HHF was underpinned by three guiding principles:

- Total well-being encompasses the physical, mental and social health of students and not just measures of weight and fitness.
- Inclusion advocates that every student be given opportunities to access the knowledge, and develop the skills and attitudes to live healthily, and
- Quality delivery involves building the capacity of teachers through professional development and engaging qualified and competent para-educators to teach holistic health effectively.

The HHF focused on the total well being of each student in a holistic manner. In addition, opportunities were given to students to develop the skills and attitudes to live healthily and sustain a healthy lifestyle even after they leave school. The HHF encompassed the formal and non-formal curricula. Formal curriculum included health education and physical education while the non-formal curriculum comprised co-curricular activities, enrichment programmes and life skills. Under the HHF, schools would engage the support of their stakeholders in health promotion since the total well being of school children is a shared responsibility of parents, schools and the community (146).

### **3.4 Ministry of Health**

#### **3.4.1 National Health Survey 2010**

The National Health Survey (NHS) is part of the Ministry of Health's on-going surveillance of the health status of Singapore. It provides regular information on the prevalence of major non-communicable diseases such as diabetes mellitus and hypertension and related risk factors like obesity and smoking from a representative sample of the resident population. Recently, the NHS has also begun to capture information on the practice of chronic disease screening, use of primary healthcare services, mental health and self-rated overall health. The latest NHS 2012 captured, for the first time, data on caregiving, hearing loss and renal impairment among Singapore residents (21).

The NHS 2010 was the fourth in a series of surveys conducted once every six years to assess and monitor the health of the Singapore population. Data collection procedures have been previously described elsewhere (147) so key aspects and the data collection procedures of the survey are repeated here for the purposes of informing the reader of this thesis.

The NHS 2010 covered non-institutionalised Singapore residents (Singapore citizens and permanent residents). The sampling plan followed a multistage design. At the first stage, sampling divisions within close proximity of the designated survey sites were chosen. Dwelling units of each selected sampling division were then stratified by house-type and systematically selected at the second stage. The eventual sample was representative of the house-type distribution of the whole housing population in Singapore.

All selected households were notified by post. Thereafter, house visits were made to enumerate all members of the households who fell within a specified age range. In the final stage, a disproportionate stratified sampling design was used to select a random sample of 7,500 individuals who were identified during the enumeration exercise. These individuals were first stratified by age and ethnic group and then systematically selected.

Prior to the commencement of data collection fieldwork, an invitation letter was mailed to each of the 7,500 selected survey participants. The invitation letter provided information on the survey appointment date, time, venue and fasting instructions. Reminder letters were sent and phone calls made nearer to the participants' appointment dates. On the actual day of the survey, participants were expected to go to their appointed survey sites where they were required to give their consent to participate in the survey. Participants then underwent a health screening and a face-to-face interview using a structured questionnaire.

### **3.5 Ethics approval for this PhD research**

Pursuant to the public sector data protection principles listed in the HPB's Data Protection Policy and other relevant ethical considerations, the following measures would be in place for the entire duration of this PhD research:

- Only de-identified secondary data would be provided to the HPB principle investigator for analysis.
- All necessary administrative and legal provisions would be instituted to ensure adequate protection of the confidentiality of all data.

- All respondents of NHS 2010 had previously signed informed consent forms agreeing that the “Ministry of Health may perform data linkage between the information collected in the survey and information about themselves in its own databases such as the National Registry of Diseases Office, electronic medical records of public sector hospitals, or other government databases such as the Births and Deaths Registry; the information obtained from this data linkage would only be used to assess the health of Singapore’s population and/or to plan and develop national health policies and programmes.”
- All parents/guardians of students who undergo school health screening conducted by HPB had provided informed consent agreeing “any information which was provided, results and follow-up activities from the health screening will be kept confidential and will only be shared with the relevant school authorities and other healthcare providers. The health information might also be collated and used for national public health policy planning, ethically approved research, official reports and publications. Full confidentiality is ensured.”
- All findings would be reported in aggregate and no individuals would be named. All principle investigators would not have any form of direct or indirect access to the identifiers of any data set from HPB, MOH and MOE.
- All findings from the research study would be shared with HPB, MOH AND MOE for policy planning and programme development. Only relevant results would be published as part of a PhD thesis of the HPB principle investigator.

### **3.6 Thesis data sources**

This thesis utilised the following data sources:

- HPB SHS dataset – 1990 to 2011
- MOE TAF dataset – 1997 to 2011
- MOH NHS 2010 (selected subset)

#### **3.6.1 SHS dataset**

The first set of data used in my research was the School Health Service (SHS) database from Health Promotion Board. This dataset routinely captured information from an on-going annual health screening dataset of school children in all primary schools (for ages 7 to 12) and 95% of all secondary schools (for ages 13 to 16) in Singapore. Data were computerised from 1990 to 2011 while paper archives were available for earlier years. Annually, about 44,000 new student records were added since 2000. In 2010, there were a total of 263,906 students in 173 primary schools and 214,388 students in 155 secondary schools (97, 98).

In SHS examinations, basic measurements (height & weight) were taken to allow the student's height percentile, weight percentile, BMI, BMI percentile and growth velocity within the year cohort to be calculated. Vision and audiometry tests were also conducted as well as mandatory vaccinations. A primary physician conducted basic screening to check on heart, lung capacity as well as assessing the growth of the student, for example, puberty staging. A trained nurse measured weight and height.



Growth charts, by weight, height and BMI, for boys and girls from ages 6 to 18 were available for classification description of weight status (92). The cut-offs were: youth with BMI scores falling  $\geq 97$ th Percentile were severely overweight; 90th to  $< 97$ th Percentile were overweight; 5th to  $< 90$ th Percentile were acceptable weight; 3rd to  $< 5$ th Percentile were underweight and  $< 3$ rd Percentile were severely underweight. It was also important to note that for the same amount of body fat as Caucasians who had a BMI of  $30 \text{ kg/m}^2$  (cut-off for obesity as defined by WHO), the BMI cut-off points for obesity would have to be about  $27 \text{ kg/m}^2$  for Chinese and Malays and  $26 \text{ kg/m}^2$  for Indians in Singapore. This was due to an observed paradox of low body mass index and high body fat percentage in the Singapore population (99, 100).

### **3.6.2 TAF dataset**

The second set of data for my research was the Trim and Fit (TAF) database from the Ministry of Education. This dataset similarly captured information routinely collected from an annual health screening dataset of school children in all primary schools (for ages 6 to 12) and 95% of all secondary schools (for ages 13 to 16) in Singapore. However, data were computerised from 1997 to 2011 only.

Physical education teachers were trained to take basic measurements (height & weight) using calibrated weighing and height measurement machines. Students who were found to be underweight or overweight or obese were referred to the Nutrition Centre at the Health Promotion Board School Health Service centre for follow-up. In addition, those who were obese were enrolled into the TAF programme, as previously described.

### **3.6.3 NHS2010 dataset**

The Global Health Questionnaire (GHQ)-12 was used, as part of a larger structured survey questionnaire; to measure mental health well-being during the face-to-face interviews with Singapore residents aged 18 to 69 in the National Health Survey (NHS) 2010. Cut-offs for poor mental health (score larger than 3) was based on an earlier validation MOH study conducted in 2003 (21).

De-identified data identifying NHS 2010 respondents as “normal” or “poor” mental health status was provided for this analysis.

## **3.7 Data preparation**

This section describes the key steps of data cleaning and preparation for subsequent statistical analysis in the thesis, which included employing latent growth and mixture analysis using Mplus. Mplus is a latent variable modelling program with a wide variety of analysis capabilities (148) and would be used as the main statistical software, together with Stata (149).

### **3.7.1 General procedures**

Both TAF and NHS2010 requested data was shared and physically sent directly to the IT consultant at HPB, in the electronic form of excel files for raw data recorded in each respective year of school-based weight and height screening by MOE and MOH. Within HPB, an external third party data vendor was contracted to merge the three data sets: SHS, TAF and NHS2010, in accordance to the study protocol to create two Master Datasets A and B. The former would be used for the purposes of Chapter Four, Five and Six and the latter was used for the purposes of

Chapter Seven. Table 27 shows the number of records and type of independent variables in both SHS and TAF (thesis data sources) and the combined Master Dataset A.

**General procedures of the first data linkage for Master Dataset A:**

1. MOE will provide identified individual data to HPB IT Department.
2. HPB will send the SHS (from HPB) and TAF (from MOE) data to a third party data vendor for data management
3. The third party vendor will link SHS and TAF data by individual student unique NRIC number combined into a Master Dataset A.
4. All identifiers will be striped from the Master Dataset A.
5. The de-identified Master Dataset A will be sent to the HPB principle investigator.

**General procedures of second data linkage for Master Dataset B:**

6. MOH will provide a list of identifiers (NRIC numbers) of only NHS 2010 respondents aged 18 to 26 years, to HPB.
7. The third party data vendor will independently link the SHS and TAF data records of these individuals (obtained from Master dataset A) and submit their linked data sets to MOH.
8. MOH will add outcome variable data from NHS 2010 of these individuals and send it back to HPB.
9. All identifiers will be stripped from the Master Dataset B.
10. The de-identified Master Dataset B will be sent to the HPB principal investigator.

It is important to note that a unique random record identifier was allocated to each student NRIC number (Singapore National Identity Card) so that every record of the same student, regardless of whether his or her data was captured during HPB health screening programme or MOE TAF programme at his or her school, would be linked at the individual level across the different ages that his or her weight/height was recorded during the entire schooling period from age 7 to 17. In some cases, data were captured for other ages as well. Table 28 shows an example of how BMI data for an individual record could be linked across ages from different data sources by their unique identifier.

**Table 27 Number of records and type of independent variables available in School Health Service, Trim and Fit (thesis data sources) and those included in Master Dataset A**

Variables	SHS	TAF	Master Dataset A
Unique ID	*	*	*
Age	*	*	*
BMI	*	*	
Postal code	*		
Gender	*	*	*
Race group	*	*	*
School code	*	*	
Education level	*	*	
House type (in 2005 2010 only)		*	
BMI z-scores			*
BMI categories			*
Father's race group	*		
Mother's race group	*		
Nutritional status	*		
Birth order	*		
Total records (n)	8,686,249	7,667,013	2,711,088

Notes:

\* – Variable is available in data source

**Table 28 An example of how BMI data for an individual record is linked across ages by their unique identifier combining data from different data sources in Master Dataset A**

Age	7	8	9	10	11	12	13	14	15	16
Education level <sup>a</sup>	P1	P2	P3	P4	P5	P6	Sec 1	Sec 2	Sec 3	Sec 4
Data available	*	N/A	*	*	*	N/A	*	N/A	*	N/A
Source	SHS	N/A	TAF	TAF	SHS	N/A	TAF	N/A	TAF	N/A

Notes:

<sup>a</sup> Education level refers to Primary (P) and Secondary (Sec) academic levels at time of physical examination

\* – Data is available

N/A – Data is not available

**Table 29 Number of records available per year in both School Health Service and Trim and Fit data sources**

Year	First source of data	Number of Records	Second source of data	Number of records
1990	SHS	446,476		
1991	SHS	483,749		
1992	SHS	486,058		
1993	SHS	481,875		
1994	SHS	484,531		
1995	SHS	502,632		
1996	SHS	516,396		
1997	SHS	438,273	TAF	471,440
1998	SHS	532,859	TAF	475,154
1999	SHS	560,624	TAF	493,286
2000	SHS	538,967	TAF	503,649
2001	SHS	537,970	TAF	512,582
2002	SHS	585,953	TAF	519,454
2003	SHS	531,045	TAF	530,156
2004	SHS	203,750	TAF	535,793
2005	SHS	207,340	TAF	531,684
2006	SHS	199,557	TAF	530,621
2007	SHS	206,128	TAF	528,807
2008	SHS	238,518	TAF	521,813
2009	SHS	174,905	TAF	515,100
2010	SHS	161,569	TAF	504,660
2011	SHS	167,074	TAF	492,814

Notes:

SHS – School Health Service dataset from the Health Promotion Board

TAF – Trim and Fit dataset from the Ministry of Education

### 3.7.2 Data merge

Annual records of SHS and TAF were provided to an external third party data vendor to be de-identified by replacing the students' NRIC numbers with a unique record identifier string number. As listed in Table 29, annual SHS data were available from 1990 to 2011 from HPB and TAF data available from 1997 to 2011 from MOE, totalling 16,353,262 student records. Subsequently, 37 Microsoft Excel files (each between 200,000 to 500,000 rows of records, each row representing one student with one BMI measured at a certain age) were sent to me and the following steps were taken to clean and merge all the data into one single dataset for further statistical analysis:

1. Estimate student's age
  - a. The student's age had to be estimated, as this was not provided, from the raw data sets. This was derived for each student in SHS and TAF, based on the educational levels code, which were recorded during the school health screening (Table 30). The ages for male and female were different at pre-matriculation into university as boys are required to undergo two and a half-years of mandatory national service in the military at age of 18 and for most boys, the age at which they would enter university would be 21 as compared to girls at 19.
2. Determine race group
  - a. Coding for race group had to be standardised and recoded between SHS and TAF datasets as different labels were used (Table 31).

**Table 30 Estimated age at each academic level in Singapore for females and males**

<b>Code</b>	<b>Description</b>	<b>Age (Female)</b>	<b>Age (Male)</b>
<b>N1</b>	Nursery 1	3	3
<b>N2</b>	Nursery 2	4	4
<b>K1</b>	Kindergarten 1	5	5
<b>K2</b>	Kindergarten 2	6	6
<b>11</b>	Primary 1	7	7
<b>12</b>	Primary 2	8	8
<b>13</b>	Primary 3	9	9
<b>14</b>	Primary 4	10	10
<b>15</b>	Primary 5	11	11
<b>16</b>	Primary 6	12	12
<b>31</b>	Secondary 1	13	13
<b>32</b>	Secondary 2	14	14
<b>33</b>	Secondary 3	15	15
<b>34</b>	Secondary 4	16	16
<b>35</b>	Secondary 5	17	17
<b>41</b>	Pre-U 1	17	17
<b>42</b>	Pre-U 2	18	18
<b>43</b>	Pre-U 3	19	19
<b>91</b>	Registered For Primary One	7	7
<b>99</b>	Others	999*	999*
<b>50</b>	Pre-matriculation	19	21
<b>51</b>	University Year 1	19	21
<b>52</b>	University Year 2	20	22
<b>53</b>	University Year 3	21	23
<b>54</b>	University Year 4	22	24
<b>55</b>	University Year 5	23	25

Notes:

\* - For the purposes of this thesis, students who had a record of “Others” for their academic levels were coded as 999 and will be excluded from statistical analysis

**Table 31 Categorical variable labels assigned to students belonging to different race groups**

<b>Code</b>	<b>Race Groups</b>	<b>Categorical variable labels</b>
<b>CN</b>	Chinese	0
<b>MY</b>	Malay	1
<b>EU</b>	Eurasian	2
<b>ID</b>	Indonesian	3
<b>IP</b>	Indian/Pakistani/Sri Lankan	4
<b>XX</b>	Others	5

3. Calculate BMI
  - a. Body Mass Index (BMI) was calculated based on the formula of weight (in kilograms) divided by the square height (in meters).
4. Remove outliers of BMI
  - a. Records with BMI values greater than 99 and less than 10 were removed
5. Remove duplicates of BMI
  - a. In order to address multiple measurements of BMI of a student who had been screened by both SHS and TAF in the same year, plus the need to establish a long form of the data structure for latent growth and mixture analysis in Mplus later on, a Power Pivot table was created using unique record IDs and averaged BMI data for each year and data source.
  - b. 37 separate Excel files containing the pivot table output of IDs and BMI measurements for age 6 to 25 were created.
  - c. Given the 1 million rows limitation in Microsoft Excel, steps 1 to 5 had to be done within each Excel file separately.
6. Combine all of SHS and TAF excel-based data into a single Microsoft Access database
  - a. In order to reduce the computing power and memory required to manipulate the 16 million rows of data, two separate procedures were used to compile the BMI only data and other student variables (age, race group, postal code, school code and gender) into two different tables within a single Microsoft Access database.
  - b. A BMIpivot table was first created in Microsoft Access by importing and appending BMI only data (wide form) from the 37 Microsoft Excel files. At this



point, each row of data represents one student ID with one BMI measurement at one age

- c. A variables table was then created for data on race and gender
- d. MOH NHS2010 data was imported into another separate table
- e. Combine and merge BMI measurements per unique student record
- f. This procedure aims to combine, merge (average duplicates), all BMI measurements of each student into a single row record
- g. An SQL query command was executed:
  - i. `SELECT BMIpivot.id AS Expr1, Avg(BMIpivot.bmi4) AS bmi4, Avg(BMIpivot.bmi5) AS bmi5, Avg(BMIpivot.bmi6) AS bmi6, Avg(BMIpivot.bmi7) AS bmi7, Avg(BMIpivot.bmi8) AS bmi8, Avg(BMIpivot.bmi9) AS bmi9, Avg(BMIpivot.bmi10) AS bmi10, Avg(BMIpivot.bmi11) AS bmi11, Avg(BMIpivot.bmi12) AS bmi12, Avg(BMIpivot.bmi13) AS bmi13, Avg(BMIpivot.bmi14) AS bmi14, Avg(BMIpivot.bmi15) AS bmi15, Avg(BMIpivot.bmi16) AS bmi16, Avg(BMIpivot.bmi17) AS bmi17, Avg(BMIpivot.bmi18) AS bmi18, Avg(BMIpivot.bmi19) AS bmi19, Avg(BMIpivot.bmi20) AS bmi20, Avg(BMIpivot.bmi21) AS bmi21, Avg(BMIpivot.bmi22) AS bmi22, Avg(BMIpivot.bmi23) AS bmi23, Avg(BMIpivot.bmi24) AS bmi24, Avg(BMIpivot.bmi25) AS bmi25 INTO BMImerge`
  - ii. `FROM BMIpivot`
  - iii. `GROUP BY BMIpivot.id;`
  - iv. Output: BMImerge table

7. Define new variable “count” for number of BMI measurements across ages 6 to 25 per student

a. This procedure aims to calculate number of BMI measurements available for each student in the database

b. An SQL query command was executed:

i. `SELECT BMImerge.id, IIf(bmi4 Is Null,0,1)+IIf(bmi5 Is Null,0,1)+IIf(bmi6 Is Null,0,1)+IIf(bmi7 Is Null,0,1)+IIf(bmi8 Is Null,0,1)+IIf(bmi9 Is Null,0,1)+IIf(bmi10 Is Null,0,1)+IIf(bmi11 Is Null,0,1)+IIf(bmi12 Is Null,0,1)+IIf(bmi13 Is Null,0,1)+IIf(bmi14 Is Null,0,1)+IIf(bmi15 Is Null,0,1)+IIf(bmi16 Is Null,0,1)+IIf(bmi17 Is Null,0,1)+IIf(bmi18 Is Null,0,1)+IIf(bmi19 Is Null,0,1)+IIf(bmi20 Is Null,0,1)+IIf(bmi21 Is Null,0,1)+IIf(bmi22 Is Null,0,1)+IIf(bmi23 Is Null,0,1)+IIf(bmi24 Is Null,0,1)+IIf(bmi25 Is Null,0,1) AS Result INTO [Count]`

ii. `FROM BMImerge;`

8. Create Master Dataset A

a. This procedure aims to select minimum number of BMI measurements available for each student in the database, merge variables on unique ID and create different new output tables. Example below shows a new output table with all students with at least 1 BMI measurement

b. An SQL query command was executed:

i. `SELECT Count.Result, BMImerge.id, BMImerge.bmi4, BMImerge.bmi5, BMImerge.bmi6, BMImerge.bmi7, BMImerge.bmi8, BMImerge.bmi9,`

BMImerge.bmi10, BMImerge.bmi11, BMImerge.bmi12,  
 BMImerge.bmi13, BMImerge.bmi14, BMImerge.bmi15,  
 BMImerge.bmi16, BMImerge.bmi17, BMImerge.bmi18,  
 BMImerge.bmi19, BMImerge.bmi20, BMImerge.bmi21,  
 BMImerge.bmi22, BMImerge.bmi23, BMImerge.bmi24,  
 BMImerge.bmi25, RaceFemale.race, RaceFemale.female INTO 7bmi

- ii. FROM (BMImerge INNER JOIN [Count] ON BMImerge.id = Count.id)  
 INNER JOIN RaceFemale ON (Count.id = RaceFemale.id) AND  
 (BMImerge.id = RaceFemale.id)
- iii. WHERE (((Count.Result)>1));
- iv. Output: AllBMI table

#### 9. Link MOH unique ID to BMI data

- a. This procedure aims to join BMI values to MOH unique ID (from NHS2010)
- b. An SQL query command was executed:
  - i. SELECT MOHID.id, BMImerge.bmi4, BMImerge.bmi5,  
 BMImerge.bmi6, BMImerge.bmi7, BMImerge.bmi8, BMImerge.bmi9,  
 BMImerge.bmi10, BMImerge.bmi11, BMImerge.bmi12,  
 BMImerge.bmi13, BMImerge.bmi14, BMImerge.bmi15,  
 BMImerge.bmi16, BMImerge.bmi17, BMImerge.bmi18,  
 BMImerge.bmi19, BMImerge.bmi20, BMImerge.bmi21,  
 BMImerge.bmi22, BMImerge.bmi23, BMImerge.bmi24,  
 BMImerge.bmi25 INTO MOHmerge
  - ii. FROM BMImerge INNER JOIN MOHID ON BMImerge.id = MOHID.id;

iii. Output: MOHmerge table

#### 10. Create Master Dataset B

a. This procedure aims to create a dataset with MOH ID, BMI values and MOH data from NHS2010

b. An SQL query command was executed:

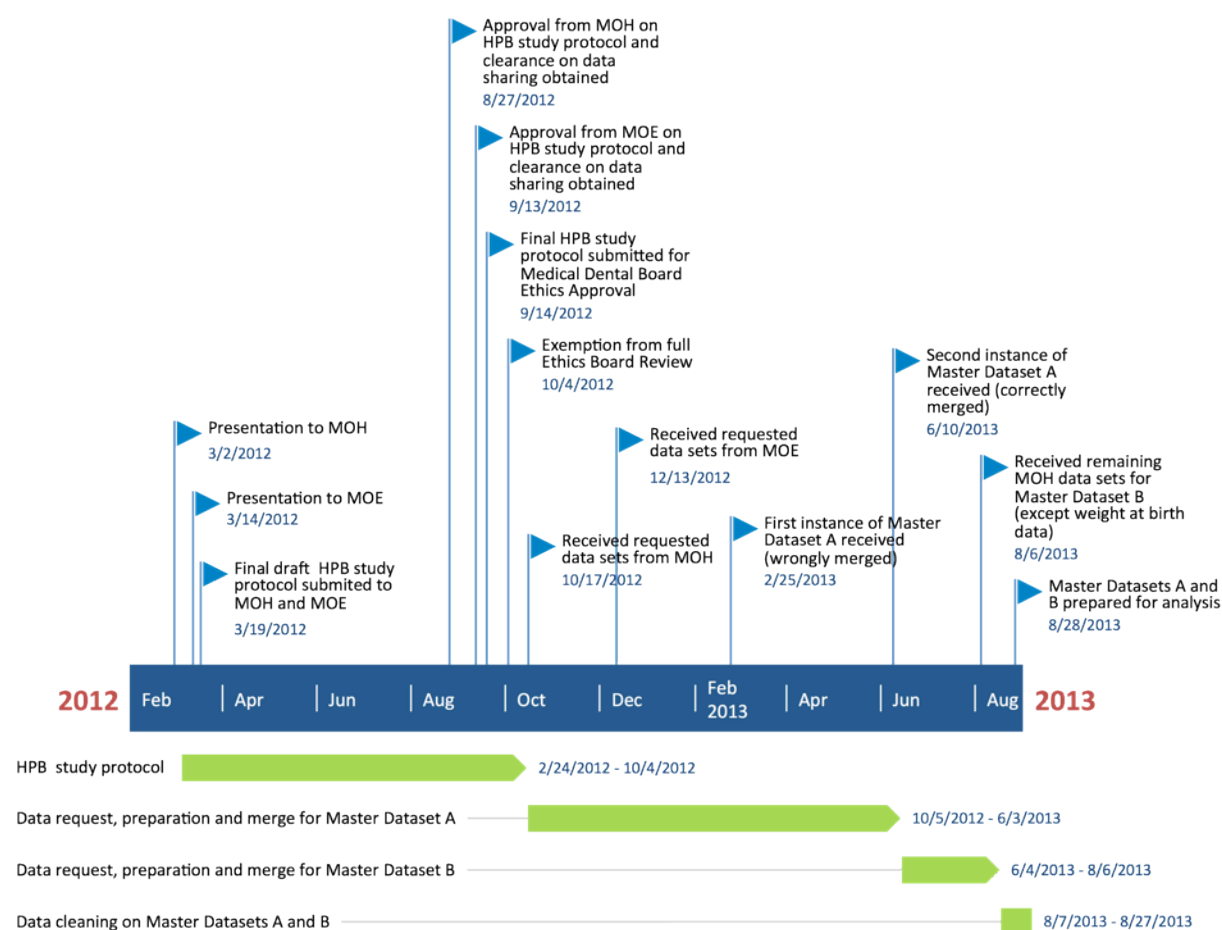
- i. `SELECT MOHdatamerge.id, MOHdatamerge.age, MOHdatamerge.race, MOHdatamerge.female, MOHmerge.bmi4, MOHmerge.bmi5, MOHmerge.bmi6, MOHmerge.bmi7, MOHmerge.bmi8, MOHmerge.bmi9, MOHmerge.bmi10, MOHmerge.bmi11, MOHmerge.bmi12, MOHmerge.bmi13, MOHmerge.bmi14, MOHmerge.bmi15, MOHmerge.bmi16, MOHmerge.bmi17, MOHmerge.bmi18, MOHmerge.bmi19, MOHmerge.bmi20, MOHmerge.bmi21, MOHmerge.bmi22, MOHmerge.bmi23, MOHmerge.bmi24, MOHmerge.bmi25, MOHdatamerge.Cho_incr, MOHdatamerge.DailySmk_incr, MOHdatamerge.DM_incr, MOHdatamerge.GHQ12_group, MOHdatamerge.Hyptn_incr INTO MOHdataBMImerge`
- ii. `FROM MOHdatamerge INNER JOIN MOHmerge ON MOHdatamerge.id = MOHmerge.id;`
- iii. Output: MOHdataBMImerge table

#### 3.7.3 Timeline

The study protocol was developed on the 24<sup>th</sup> February 2012 and finalized on the 4<sup>th</sup> of October 2012 after a series of consultative meetings and revisions by the Health Promotion

Board, the Ministry of Education and the Ministry of Health. Data request and preparation for Master Dataset A took approximately five months to complete and data request to MOH and preparation for Master Dataset B took approximately two months to complete. Final steps in data cleaning on both Master Dataset A and B were completed within a month. Figure 2 shows the key milestones during study protocol development, data request, merge and final preparations.

**Figure 2 Timeline for development of study protocol, data request and preparation for the thesis (Feb 2012 to Aug 2013)**



### **3.8 Conclusion**

The final outcome of data preparation was a dataset that represented the largest pooling of anthropometric data from about 2.7 million individuals born from 1973 to 2003 collected through routine school-based health screening in Singapore from 1990 to 2011 by HPB and MOE. Details on the basic summary statistics of the final datasets will be described in the next Chapter.

## **Chapter 4: Cohort profile of the Singapore Longitudinal and Life Course Cohort (SLLCC)**

### **Synopsis**

An extensive dataset of repeatedly measured anthropometric data of about 2.7 million students (48% female) was created in Chapter Three by merging data from two separate school-based health screening programmes in Singapore with appropriate data preparation steps. This data set is named as a new Singapore Longitudinal and Life Course Cohort (SLLCC).

Briefly, 1,013,316 students (37.4% of total SLLCC data set) had their Body Mass Index (BMI) measured five or more times within their primary and secondary schooling life. Sex-specific BMI-for-age z-scores were standardised for all students using WHO Child Growth Standards. Lowest median BMI z-scores (-0.35) were observed at age 16 and highest at age 11 (0.36). Ethnic race breakdown was 72.2% Chinese, 13.3% Malays, 8.1% Indians, 6.2% others. Other variables available in SLLCC included year of health screening, birth cohort, type of housing and school attended.

One of the main rationales for establishing the SLLCC as part of the PhD research programme is to address the shortcomings of previous studies on weight change in Chapter Two, for example, limitation by measurements of weight change over two time points only, as compared to modelling the entire trajectory of change over repeatedly measured anthropometric measurements as a determinant for future or later life outcomes. The extensive national coverage (about 95%) of students physically examined from 1990 to 2011 from age 7 to 16 would permit data exploration using the life course conceptual framework and techniques such as latent growth curve modelling (Chapter Five, Six and Seven). Also, by making available disaggregated data by

age, period and birth cohort, more in-depth analysis of the obesity secular trends among school-age children may be attempted (Chapter Five).

But first, in this Chapter Four, I will present the epidemiological profile of the full SLLCC cohort including providing information on data variables that are available; characteristics of the cohort; its strengths and weakness; finally, instructions for requesting access to the data sets.

## **4.1 Background**

### **4.1.1 Context**

Obesity is on the rise in Singapore in the last decade with the prevalence of obese adults being 10.8% in 2010, representing a significant increase from 6.9% in 2004. Among its three major ethnic groups, Malays have the highest prevalence of 24%, followed by Indians (16.9%) and Chinese (7.9%) (21). Understanding the public health implications of this trend of increasing BMI is important for countries due to its propensity to reduce human lifespan and increase the risks of cardiovascular diseases and other chronic morbidities in later life (2).

To date, Singaporean longitudinal studies of obesity are limited (150-154). Given that obesity is a well known risk factor for the development of chronic diseases such as cardiovascular diseases and diabetes (103, 104), there are, however, a few notable cohort studies or programs that aimed to disentangle causal or associative relationships between exposure risk factors such as obesity or other metabolic indicators with all-cause or other disease specific outcomes in Singapore.



To begin with, I would like to present a summary of the existing longitudinal cohorts in Singapore that are relevant to obesity research before providing a rationale for assembling the new Singapore Longitudinal and Life-Course Cohort (SLLCC).

#### **4.1.2 Summary of Singapore Cohorts**

##### ***4.1.2.1 Introduction***

Firstly, it is important to point out that almost all recently published cohort research (described in this Chapter) related to obesity in Singapore were based on selective pooling of various cross-sectional national surveys, in which respective participants, mostly adults, were contacted for subsequent follow-up health screening or monitoring of particular chronic conditions. Briefly, these surveys included a random sample of individuals from the Singapore population, with disproportionate sampling stratified by ethnicity to increase the number in the minority ethnic groups (Malays and Indians). Although their clinical objectives were different, the surveys had common data collection instruments and comparable clinical assessment protocols, including anthropometric measurements, such as weight and height, to allow merging of datasets. Table 32 presents a summary of selected longitudinal studies relevant to the study of obesity in Singapore.

**Table 32 Summary of selected longitudinal cohorts relevant to the study of obesity in Singapore**

<b>Cohort name (year established)</b>	<b>Size</b>	<b>Data sources</b>	<b>Primary research objective</b>
<b>Singapore Cardiovascular Cohort Study (2000)</b>	5,920	Thyroid and Health Survey 1982-1984, National Health Survey 1992 and National University of Singapore Heart Study 1993-1995	To study incidence of ischemic heart disease and stroke among Chinese, Malays and Asian Indians
<b>Singapore Prospective Study Program (2007)</b>	10,445	Thyroid and Heart Study 1982-1984, National Health Survey 1992, National University of Singapore Heart Study 1993-1995, and National Health Survey 1998	To examine the pathogenesis of cardiovascular and metabolic diseases (hypertension, dyslipidemia, obesity, and diabetes mellitus)
<b>Singapore Consortium of Cohort Studies (2007)</b>	9,217	NUS Diabetes Cohort Study, Singapore Prospective Study Program, and Singapore Cardiovascular Cohort Study 2	To investigate the genetic and lifestyle factors affecting the risk of developing various chronic diseases such as diabetes, cancer, and heart disease
<b>Singapore Diabetes Cohort (2010)</b>	Over 5,000	Individuals (with Type 2 Diabetes) recruited from National Healthcare Group Polyclinics, National University Hospital Singapore and the Tan Tock Seng Hospital	To identify genetic and environmental risk factors for diabetic complications.
<b>Singapore Cohort study Of the Risk factors for Myopia (1999-2001)</b>	1,979	Healthy children from grades 1-3 (age 7 to 9) who were recruited from three schools in Singapore (located in the Eastern, Western and Northern regions)	To determine the risk factors of incident myopia in a school-based cohort
<b>Growing Up in Singapore Towards healthy Outcomes (2010)</b>	1,163	Healthy pregnant women were recruited in their first trimester and subsequently their offspring would be part of the study	To evaluate the role of developmental factors in the early pathways to metabolic compromise, namely obesity and Type 2 Diabetes Mellitus.

#### ***4.1.2.2 Singapore Cardiovascular Cohort Study***

The Singapore Cardiovascular Cohort Study (SCS) was the first prospective cohort study in Singapore to describe the incidence of ischemic heart disease (IHD) and stroke among Chinese, Malays and Asian Indians in 2000. A total of 5,920 people, of which 2,920 were male, comprised the cohort, composed of participants from three previous cross-sectional surveys: the Thyroid and Health Survey 1982-1984, the National Health Survey 1992 and the National

University of Singapore Heart Study 1993-1995. Morbidity and mortality from IHD and stroke were ascertained by record linkage using a unique identification number with the death registry, Singapore Myocardial Infarct Registry and in-patient discharge databases (155).

Subsequently, the cohort was followed up over 10 years for a number of other outcome measures, such as for relationships of established coronary risk factors with incident coronary heart disease (156), the effect of pre-hypertension (157), hypertension alone, and in combination with other CVD risk factors on all-cause and CVD mortality (158).

#### ***4.1.2.3 Singapore Prospective Study Program***

The Singapore Prospective Study Program (SP2) was a cross-sectional study of adult Singaporean Chinese, Malay and Asian-Indian samples, aged between 24 to 95 years. The methodology of constructing the study sample has been described in detail elsewhere (159). Briefly, 10,445 subjects from 4 population-based, cross-sectional surveys conducted in Singapore (1982–1998) were invited to participate in a repeat examination from 2004 to 2007. The four studies include the Thyroid and Heart Study 1982–1984, the National Health Survey 1992, the National University of Singapore Heart Study 1993–1995, and the National Health Survey 1998. A total of 7,742 (74.1% response rate) subjects completed the investigator-administered questionnaire at their homes; 5,157 of them (66.6% of those who completed the questionnaire or 49.4% of all eligible subjects) also attended an in-person health examination.

The availability of a large number of healthy participants has offered the opportunity for researchers to examine the relation between fasting plasma glucose and the prevalence of chronic

kidney disease and peripheral neuropathy in a large population spanning the full range of glucose tolerance (159). Participants from the SP2 have also been followed up to explore and compare health-related quality of life levels in the three main ethnic groups in Singapore: Chinese, Malay, Indian (159).

#### ***4.1.2.4 Singapore Consortium of Cohort Studies***

The Singapore Consortium of Cohort Studies (SCCS) was a research initiative funded by the Biomedical Research Council (BMRC). This large prospective study aimed to investigate the genetic and lifestyle factors affecting the risk of developing various chronic diseases such as diabetes, cancer, and heart disease. The SCCS is composed of two major arms, a diabetic cohort (DC), and a multi-ethnic cohort (MEC). The DC will build on the existing NUS Diabetes Cohort Study of 3,900 diabetic patients who were previously recruited. The MEC is a cohort of normal people aged 21 to 75 who will be followed up in 3-5 year intervals for the development of a wide range of diseases. The MEC builds on two existing cohort studies, the Singapore Prospective Study Program (SP2), and the Singapore Cardiovascular Cohort Study 2 (SCCS2). At the end of July 2007, there were a total of 5,214 subjects in the MEC and 4,003 patients in the DC (160).

Essentially, the SCCS was a national effort to pool selected cohort studies and build on these to develop a large multi-ethnic population-based cohort study to facilitate research into the complex gene-environment interactions in diseases such as diabetes, cardiovascular diseases and cancers. It also served to provide a large variety of healthy controls, which can be matched with regards to age or ethnicity for current on-going case-control studies (160).

#### ***4.1.2.5 Singapore Diabetes Cohort***

The Singapore Diabetes Cohort (SDCS) included Singaporean Chinese, Malay, and Asian-Indian adults with type 2 diabetes and had been published previously (161). These individuals were recruited from National Healthcare Group Polyclinics, National University Hospital Singapore and the Tan Tock Seng Hospital. The study had a participation response rate of 90% with over 5,000 patients recruited.

#### ***4.1.2.6 Singapore Cohort study Of the Risk factors for Myopia***

The Singapore Cohort study Of the Risk factors for Myopia (SCORM) (162) is a prospective study consisting of 1,979 children from grades 1-3 (age 7 to 9) who were recruited from three schools in Singapore (located in the Eastern, Western and Northern regions). Children with serious medical conditions such as heart disorders and leukaemia were excluded from the study (n=94). BMI measures were taken at each annual follow up visits.

#### ***4.1.2.7 Growing Up in Singapore Towards healthy Outcomes***

Growing Up in Singapore Towards Healthy Outcomes (GUSTO) is Singapore's largest and most comprehensive birth cohort study to date (163). With recruitment commencing in 2009, it is a currently on-going cohort study of pregnant women and their offspring, with recruitment beginning in the first trimester. The last GUSTO baby was born in May 2011. Mothers have been followed throughout pregnancy and their offspring will be examined until the child reaches 3 years of age. It is currently planned to continue follow-up through childhood and into adulthood.

The primary objective of the GUSTO birth cohort study is to evaluate the role of developmental factors in the early pathways to metabolic compromise, namely obesity and Type 2 Diabetes Mellitus. Recruitment for the study was completed in September 2010 with 1,163 pregnant women recruited into the main GUSTO cohort (current drop-out rate = 12.1%). All of the women have delivered but data collection and analyses are still on-going. Amongst the participants recruited, 56% were Chinese, 26% Malay and 18% Indian. Of the babies delivered, at least 945 have reached 3 months of age by end-May 2011 (164).

The GUSTO study adopted a novel methodology to examine (in relation to clinical outcomes) the epigenetic effects of maternal diet, in addition to epigenetic markers at birth as a function of foetal growth and subsequently over development and its effect on allergy and other domains such as nutrition, prematurity, fertility, pregnancy, eye dental health and cognition. A unique feature of GUSTO is that the three distinct ethnic groups, Chinese, Malays and Indians, in the Singaporean population allows in-depth examination of the extent to which genomic variation influences allergic phenotype (164).

## **4.2 SLLCC cohort profile**

### **4.2.1 Why was this new cohort established?**

It is clear that there are negative implications of several early life factors on adult health in general and these have been well researched. Whilst there is also good evidence supporting tracking of obesity (55), food consumption and physical activity from childhood to adulthood (63), the evidence on the long-term effects of weight gain or loss (BMI changes) through the life course associated with risk of later life outcomes is not clear.

The life course approach offers a new framework for exploring how socially patterned exposures during childhood, adolescence, and early adult life influence adult disease risk and socioeconomic position, and hence may account for social imbalances in adult health and mortality (53). Socioeconomic factors at different life stages may operate either via social chains of risk or by influencing exposures to causal factors at earlier life stages that form part of long term biological or psychological chains of risk. Many of the suggested behavioural and social risk factors are highly correlated, or may operate as proximal and distal etiological factors on the same causal pathways (40, 165).

Investigating associations between anthropometric change or fluctuations and mortality or morbidity is particularly challenging and requires sufficiently long term follow up in order to permit exclusion of early deaths so as to disregard likely effects of illness-related weight loss. This is often referred to as a “temporal separation” between periods of anthropometric change measurements and of follow up for outcomes (see Chapter One). Several other factors such as time period over which weight change is measured, methods used to define weight change, period of life during which weight change is measured, classification of body mass index, confounding by smoking, intentional weight loss and pre-existing morbidities, all make interpretations and comparisons of results from cross-sectional studies difficult.

There are also problems with past statistical methods or research designs, especially the observations of studies that mostly only employ two time points. This type of anthropometric change study design is not ideal for studying development because the collection of individual

trajectories is limited to a collection of straight lines. While two observations of BMI or equivalent anthropometric measures such as waist circumference or waist-hip ratio provide information about the amount of change, they address other research questions quite poorly. For example, is individual change linear or non-linear? Is it consistent over time or does it fluctuate? Are there sub-groups of individuals who share unique distinct developmental trajectories compared to the population mean trajectory?

More recent analytical techniques have been developed to allow researchers to conceptualise models that may provide insights and methods to better describe and compare growth and change curves over time within a life span. Some of these life course research methods provide new possibilities to model latent, pathway and cumulative effects in a conceptually coherent manner (23, 166). However, this usually requires an extensive dataset consisting of longitudinal, repeated measures of variables, sometimes including multiple cohorts, and analysing this data using various longitudinal latent variable modelling techniques such as latent growth curve models (167).

Therefore, the main rationale for establishing the Singapore Longitudinal and Life Course Cohort (SLLCC) was to develop a better understanding on the anthropometric development of children and adolescents (ages 6 to 18) in Singapore and its effects across the life course.

By making accessible an extensive individual-level dataset of repeatedly measured anthropometric data, from about 2.7 million students born between 1973 to 2003, collected through routine annual school-based health screening in Singapore from 1990 to 2011 - it is



envisioned that future investigators may apply life course epidemiological methods such as latent class analysis and finite mixture modelling in their research (73). Given that every Singapore citizen has a unique national identify card number (NRIC), there is the promising potential of additional linkages using other existing national or cohort datasets and encouraging cross-disciplinary research collaborations.

#### **4.2.2 Who is in the cohort?**

##### ***4.2.2.1 Trim and Fit (1997-2011)***

In 1992, Singapore's health ministry launched a national programme promoting a healthy lifestyle to address the common risk factors for chronic diseases such as obesity, physical inactivity, and cigarette smoking. Different age groups in the population were targeted, including school children. The Health Promotion Board (HPB) of the Ministry of Health (MOH) works in close partnership with the Ministry of Education (MOE) on obesity programmes for school children. The MOE's "Trim and Fit" (TAF) programme (See previous chapter) for primary, secondary, and pre-university schools aimed to reduce obesity in school children and improve the physical fitness of the pupils using a multi-disciplinary approach targeting overweight students, parents, teachers, and the school environment. Under the programme, schools were recognised for their efforts in improving physical fitness and reducing obesity in their schools. Each year, schools were banded according to their fitness index, results in the National Physical Fitness Award (NAPFA) test and percentage of overweight students.

The height and weight of almost all Primary and Secondary school students who had to undergo the compulsory NAPFA test were measured by a physical education teacher using

standard weighing and height machines. These anthropometric data were recorded and submitted to the MOE as part of the on-going monitoring of physical fitness and health screening under the TAF Program.

For the purposes of constructing the SLLCC, annual records of TAF from 1997 to 2011 were provided to an external third party data vendor to be de-identified by replacing the students' NRIC numbers with a unique record identifier string number. In addition, individual demographic data on gender, race, postal code of residence, date of birth, school code and educational level were added to each student record. Annually, an average of 500,000 students in 203 primary schools and 172 secondary schools were compiled in the TAF datasets (see Table 2 for the number of records per year).

#### ***4.2.2.2 School Health Service (1990-2011)***

Every year, the School Health Service (SHS) of the Health Promotion Board in Singapore conducts routine health screening for school children in all primary schools (for ages 6 to 12) and 95% of all secondary schools (for ages 13 to 16) in Singapore. In conjunction with the immunisation schedule, school nurse teams conducted general medical examinations, which included assessment of nutritional status and physical measurements of height and weight (See previous Chapter).

SHS data were computerised from 1990 to 2011 while paper archives are available for earlier years. Annually, about 44,000 new student records are added since 2000 (Table 29).

### 4.2.3 Which variables are available?

#### 4.2.3.1 *Anthropometric measures in the SLLCC*

Changes in adiposity over time can be based on the change in BMI, or the proportional (percentage) change in BMI, or the change in BMI Z-score or centile (168). In 2006, the WHO launched new growth standards for children irrespective of ethnicity, socio-economic status and feeding mode (169). By April 2011, at least 125 countries, representing 75% of the world's under-5 population, had adopted the standards and were at varying stages of their implementation (170). It is important to note that WHO standards depict how children should grow, on average, in all countries, when properly fed and cared for, rather than merely describing how they grew at a particular time and place such as use of as national/local growth references.

BMI for sex- and age-specific percentiles had been used in Singapore for ease of communicating concerns of severe underweight, overweight and severe overweight (See Chapter One for percentile classifications). However, when required to assess longitudinal growth in children, the use of percentiles is less than ideal due to inherent limitations such as same increments at different percentile levels could correspond to different changes in both Z-scores and absolute measures and it does not allow for quantifying the change in percentile values near the extremes of the reference distribution. It has been suggested that percentiles should not be used to assess change in status over time, while change in BMI Z-scores is a better measure for such research (171).

There are several advantages of using BMI z-scores over percentiles as the former are calculated based on the distribution of the reference population (both the mean and the standard deviation), thus, they reflect the reference distribution. Secondly, as standardised measures, Z-

scores are comparable across age, sex and measure. Thirdly, a group of z-scores can be subject to summary statistics such as mean and standard deviation (SD) and can be studied as a continuous variable thereby allowing quantification of the growth status of children outside of the normal percentile ranges (171).

Therefore, for the purposes of the Singapore Longitudinal and Life Course Cohort (SLLCC), sex-specific BMI-for-age z-scores were standardised for all students using the new Stata command “zanthro” (172). Briefly, this extension converted child anthropometric data to Z-scores using the LMS method and the reference data available from the 2000 CDC Growth Reference, the British 1990 Growth Reference, the WHO Child Growth Standards, the WHO Reference 2007, the UK-WHO Preterm Growth Reference, and the UK-WHO Term Growth Reference. In the SLLCC, standardised BMI-for-age Z-scores were derived from WHO child growth standards so that results can be internationally more comparable.

In addition, students were categorised as normal weight, overweight or obese using BMI categories that correspond to equivalent adult BMI cut-off points endorsed by the World Health Organization: BMI <25 kg/m<sup>2</sup> for normal weight, BMI 25–29.99 kg/m<sup>2</sup> for overweight, and BMI >30 kg/m<sup>2</sup> for obesity (Table 33).

**Table 33 WHO classification of body mass index (BMI)**

Value	Grade/Label	BMI range at 18 years
-3	Grade 3 thinness	<16
-2	Grade 2 thinness	16 to <17
-1	Grade 1 thinness	17 to <18.5
0	Normal weight	18.5 to <25
1	Overweight	25 to <30
2	Obese	30+

#### ***4.2.3.2 Race, gender and social economic position***

Gender and race had been reported to have significant early life influences for class membership in a study that identified developmental trajectories of overweight in children and adolescents (173). A cross-sectional study investigating BMI of Chinese, Malays and Indians in Singapore has consistently shown that for males there are few ethnic differences, however, for females, Malays and Indians are significantly more obese than Chinese (156), consistent with the National Health Survey 2010 findings. Findings from the Singapore Cardiovascular Cohort Study (156) show that Indians had a three fold increased relative risks of incident CHD (RR=3.1, CI: 2.0–4.8) compared with Chinese and Malays, after adjusting for age, ethnic group and other risk factors (LDL-Cholesterol, HDL-Cholesterol, Triglycerides, BMI, smoking, diabetes, hypertension and alcohol use).

It is unlikely that BMI trajectories will not be influenced by social disparities due to differential childhood social and economic status/positions (SES/SEP), commonly defined by highest educational level of the child's parent (76) or classification of parent's occupation (77) or income levels or type of housing. In the Singapore Malay Eye Study, lower SES, defined by categories of education and income were associated with higher prevalence of overweight/obesity in Malay women. In contrast, higher SES was associated with higher prevalence of overweight/obesity in Malay men (78). A prospective follow-up study of the 1998 National Health Survey on the socio-demographic determinants of changes in body weight and waist circumference in Singapore adopted highest education level, housing type and employment status as proxy measures for SES (79). In a life-course study on SES and obesity in older Singaporean Chinese men and women, childhood SES was based on the participant's (self-

reported) family financial status while growing up; adulthood SES was based on highest education attained; and older adulthood SES was based on type of housing one resides in (i.e., private or public), and within public housing, the number of rooms (ranging from 1 to 5) in the house (166). Nevertheless, there is not yet a standard index of SES or SEP in Singapore.

The SLLCC (Master Dataset A) included data on gender and race groups for all its subjects, namely Chinese, Malays, Indians, Eurasian, Indonesians and Others. Housing type data was recorded only from TAF 2005 to 2011 datasets only and thus was not included in the final SLLCC dataset but available separately. Postal codes of subjects' residence were also available for additional linkage but had not yet been geo-referenced to determine housing type (Table 27).

#### ***4.2.3.3 School-level factors***

Academic performance in schools has the potential to alter the trajectory of adult weight gain and subsequent midlife outcomes. Previous studies have reported that the odds of being persistently overweight were significantly reduced among those with a higher average grade in high school (174). The evidence also suggests that individual resources and other collective social capital operating in the school setting can attenuate the risks for obesity and overweight even among those from a lower social economic status (313).

At the time of constructing the SLLCC, there was no obvious access to individual level academic performance in schools in Singapore. One possible indirect school level factor predictor that could be the ranking of schools in Singapore based on overall academic performance.

#### ***4.2.3.4 Walkability Index***

Understanding why some people exercise more than others is a complex social and psychological challenge. Having knowledge about the general prevalence of physical activity in the population is essential in order to support interventions aimed at increasing the level of physical activity at the community or neighbourhood level. It is also necessary to help understand of the relationships between social determinants of health, physical activity and where people live.

To this end, a validated Walkability Index has been constructed in Singapore based on my Master's thesis research at the HPB in 2010. In constructing the Walkability Index for adults, 5 distinct domains driving physical activity were postulated: public transport, sports facilities, food, park connectors and community centres. The features of each domain were selected based on the ease of availability of data and its relevance to influence choice of physical activity. Two measures of social economic status (Populations living in public housing and resident working persons aged 15 years and above requiring public transportation to work) were also postulated to be predictors for walkability and included in the Index. A high score for the Walkability Index predicted the 'walkability' of a community or the extent to which characteristics of the built environment and land use may or may not be conducive to residents in the area walking for either leisure, exercise or recreation, to access services, or to travel to work. This could be used in future research as a proxy for the propensity of the school environment to encourage students to walk and serve as a potential predictor for subsequent studies.

In the SLLCC, each student record was linked to their school code at the time of health examination. In addition, each school in the dataset could be assigned a score of the Walkability Index based on the postal code of the location of the school residing within one of the 55 Development Guiding Plans (geographical zones) in Singapore. Classifications of school types (public/private and other categorical measures) and the school neighbourhood's walkability index could be determined separately as this had not yet been done in the current SLLCC datasets.

#### **4.2.4 Data preparation**

Annual records of SHS and TAF were provided to an external third party data vendor to be de-identified by replacing the students' NRIC numbers with a unique record identifier string number (see Chapter Three). Figure 3 is an illustration of the age-period-cohort schematic for SLLCC data.



Birth Cohort	Age																						
Period	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2001	2003	2004	2005	2006	2007	2008	2009	2010	2011	
2003																						6	
2004																					6	7	
2003																				6	7	8	
2002																			6	7	8	9	
2001																		6	7	8	9	10	
2000																	6	7	8	9	10	11	
1999																6	7	8	9	10	11	12	
1998															6	7	8	9	10	11	12	13	
1997														6	7	8	9	10	11	12	13	14	
1996													6	7	8	9	10	11	12	13	14	15	
1995												6	7	8	9	10	11	12	13	14	15	16	
1994											6	7	8	9	10	11	12	13	14	15	16	17	
1993										6	7	8	9	10	11	12	13	14	15	16	17	18	
1992								6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	
1991								6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	
1990							6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	
1989						6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	
1988					6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	
1987				6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	
1986			6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	
1985		6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	
1984	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	
1983	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	
1982	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	
1981	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	
1980	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	
1979	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	
1978	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	
1977	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	
1976	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	
1975	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	
1974	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	
1973	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	
1972	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	

**Figure 3 Age-period-cohort data structure of the Singapore Longitudinal and life Course Cohort (SLLCC)**

### 4.3 Characteristics of cohort

The initial total number of unique records in the Singapore Longitudinal and Life Course Cohort (SLLCC) was 2,711,108. 200 observations were dropped due to unknown gender and a total of 9,867,827 sex- and age-specific BMI z-scores were generated. Z-score values could be missing because BMI-for-age was non-positive or otherwise out of range for the chart code, the gender variable was missing, or the Z-score value had an absolute value  $\geq 5$  (extreme outliers with standard deviation more than 5 were excluded).

In Singapore, the racial breakdown of almost 3.8 million resident Singaporeans was about 74.1% Chinese, 13.4% Malays, 9.2% Indians and 3.3% others, from 2010 to 2012 (175). This

compared well with the overall ethnic race groups breakdown in the dataset, which consisted of 72.2% Chinese, 13.3% Malays, 8.1% Indians, 6.2% others. There were 52% male and 48% female students in the SLLCC (see Table 34).

**Table 34 Race and gender distribution in the Singapore Longitudinal and Life Course Cohort (SLLCC)**

	Chinese	Malay	Eurasian	Indonesian	Indian	Others	Total
<b>Male</b>	1,010,991	187,531	4,754	52,183	112,814	32,777	1,401,050
<b>Female</b>	947,509	173,106	4,620	47,273	106,658	30,872	1,310,038
<b>Total (%)</b>	1,958,500 (72.2%)	360,637 (13.3%)	9,374 (0.3%)	99,456 (3.7%)	219,472 (8.1%)	63,649 (2.3%)	2,711,088

Notes:

SLLCC consists of an extensive individual-level dataset of repeatedly measured anthropometric data, from about 2.7 million students born between 1973 to 2003, collected through routine annual school-based health screening in Singapore from 1990 to 2011.

Given that there are additional health screening efforts conducted by the SHS at age 7 (first year of Primary school), age 12 (last year of Primary school) and age 16 (last year of Secondary school), it was not surprising that there was a higher percentage of BMI being measured at those ages. There was a relatively high proportion (63%) of missing BMI measurements due to the fact that routine data collected for TAF and SHS were for operational purposes and as such are prone to inconsistency in data recording, accuracy and check for completeness (Table 35).

**Table 35 BMI Z-scores summary statistics of subjects in the Singapore Longitudinal and Life Course Cohort (SLLCC)**

BMI z-score at ages	Count	% Of total	Quantiles			No. Of missing values	% Missing
			25 <sup>th</sup>	Median	75 <sup>th</sup>		
7	1,333,403	13.5%	-1.15	-0.33	0.71	1,377,685	50.8
8	931,337	9.4%	-1.05	-0.05	1.27	1,779,751	65.7
9	950,555	9.6%	-1.01	0.11	1.47	1,760,533	64.9
10	889,339	9.0%	-0.94	0.35	1.68	1,821,749	67.2
11	885,067	9.0%	-0.96	0.36	1.66	1,826,021	67.4
12	1,334,927	13.5%	-0.88	0.18	1.32	1,376,161	50.8
13	868,823	8.8%	-0.93	0.18	1.43	1,842,265	68.0
14	842,667	8.5%	-0.98	0.01	1.21	1,868,421	68.9
15	814,283	8.3%	-1.01	-0.09	1.04	1,896,805	70.0
16	1,017,426	10.3%	-1.12	-0.35	0.56	1,693,662	62.5

Notes:

SLLCC consists of an extensive individual-level dataset of repeatedly measured anthropometric data, from about 2.7 million students born between 1973 to 2003, collected through routine annual school-based health screening in Singapore from 1990 to 2011.

Table 36 presents the effective sample sizes depending on the number of BMI measurements (z-scores) recorded for each student as they grow through ages 6 to 18. About 50% of SLLCC subjects would have between one to three BMI measurements and only 1.89% (51,105) would have their BMI measured a total of ten times within their primary and secondary schooling life.

**Table 36 Effective sample sizes based on the number of BMI Z-scores recorded from age 6 to 18 in the Singapore Longitudinal and Life Course Cohort (SLLCC)**

Number of BMI z-scores recorded	Effective Sample size (n)	% Total sample size	Cumulative %
1	911,322	33.61	33.61
2	296,904	10.95	44.57
3	282,033	10.4	54.97
4	207,504	7.65	62.62
5	207,658	7.66	70.28
6	217,613	8.03	78.31
7	167,222	6.17	84.48
8	164,614	6.07	90.55
9	179,127	6.61	97.16
10	51,105	1.89	99.04
11	25,397	0.94	99.98
12	589	0.02	100
<b>Total</b>	<b>2,711,088</b>	<b>100</b>	

Notes:

SLLCC consists of an extensive individual-level dataset of repeatedly measured anthropometric data, from about 2.7 million students born between 1973 to 2003, collected through routine annual school-based health screening in Singapore from 1990 to 2011.

#### **4.4 What are the strengths and weakness of the SLLCC?**

To the best of my knowledge, the Singapore Longitudinal and Life Course Cohort (SLLCC) is the largest longitudinal cohort of youth (ages 6 to 18) in Singapore to-date. It consists of an extensive individual-level dataset of repeatedly measured anthropometric data, from about 2.7 million students born from 1973 to 2003, collected through routine annual school-based health screening in Singapore from 1990 to 2011. The SLLCC provides valuable information regarding anthropometric developments of children and adolescents in Singapore and its effects across the life course.

The essential feature of the SLLCC is that it provides repeated observations over time on a set of variables for the set of subjects belonging to the cohort. Methodologically speaking, it is

a longitudinal cohort design by record linkages. Longitudinal data sets constructed in this manner have some significant advantages relative to the interview-based survey methods used in other cohort designs such as retrospective, birth cohorts, individual and household repeated panels (176). Firstly, the SLCC has a very large sample size of 2.7 million subjects, which means that analysis can be constructed for almost every population subgroup of interest (for example, among different ethnic race groups, gender and social economic positions) and sampling errors are minimised. Constructing the SLLCC did not require a sampling methodology to ensure statistical power as it utilised the MOE and HPB's health screening programs with a combined national coverage of 95% across all primary and secondary schools in Singapore. Essentially, one could identify almost all boys and girls in the study time period given that the mean years of schooling is between 8 to 10 since 2002 (177) and likely similar before 2002.

Secondly, by not using interviews and not depending on respondent recall, there are no additional respondent burden or recall or reporting biases (except those that cannot be validated in terms of inaccurate data entry during health screening as the data collected was not intended for research at the point of examination).

Thirdly, since the National Registration Act of 1965 (178), all Singapore citizens and permanent residents have been issued a unique NRIC number. This has great potential in the establishing individual-level linkages to several other existing national datasets such as the Singapore Census of Population, Household Surveys, both of which are rich sources of revealing additional demographic, economic, household, travel characteristics of SLLCC subjects.

The main weakness in using record linkages for research is that the range of variables is limited and constrained by the original data collected by HPB, which was originally intended for the early detection & management of health problems through health screening in schools, and in the case of the data collected by MOE, was intended for monitoring of physical fitness of students. Ideally, it would be beneficial to be able to include common social economic position variables such as housing types, parents' highest educational level and smoking status, income, and other economic factors in both statutory programs.

Examples of similar SLLCC cohort design in other countries include the Finnish Longitudinal Census File (179) and the Danish Longitudinal Database (180).

#### **4.5 Accessibility of the data**

The Singapore Health Promotion Board has a process for requesting data and research collaborations. This information can be found on [www.hpb.gov.sg](http://www.hpb.gov.sg). All requests are usually reviewed by the Department of Research and Strategic Information and proposals should fulfil criteria that stipulate clearly the aims, statistical analysis and data required. Ethics approval through the Medical Dental Board of Singapore is necessary for all research proposals requesting use of SLLCC data.

#### **4.6 Conclusions**

Administrative and routinely collected data are important sources of information. It is widely recognised that these data have immense potential value for research across a wide range of subject areas. The value can be even greater when data are securely linked, with participant

consent, to other longitudinal survey or cohort data. Launched on 1 October 2012, the Cohorts and Longitudinal Studies Enhancement Resources (CLOSER) is a consortium of the UK's leading birth cohort and longitudinal studies. It aims to maximise the use, value and impact of these studies both within the UK and abroad (181). This is a valuable approach that might be relevant in Singapore.

Since the Singapore Longitudinal and Life Course Cohort (SLLCC) has been established for this thesis, it would be important to consider how other data sets can be linked to it in the future. Similar to other developed economies, Ministries and public sector civil departments in the Singapore Government routinely collect data on various aspects of life: children's academic performance through the education system, information about social benefits claimed and income taxes paid, public/private hospital admissions and primary/secondary/specialists health care utilisations, among other administrative data. Most would agree that these data have immense potential value for research across a wide range of subject areas that have potential impact on general and priority subpopulations (such as youth and populations of low socioeconomic status). An evidence-informed policy-making process will also enhance positive impact on health outcomes.

The strength of the SLLCC is the ability for anthropometric changes of school-age children to be analysed by birth cohort and calendar year. If information across various data sets can be harmonised (recoding or modifying variables so that they are comparable across various longitudinal studies), it would be possible to undertake cross-cohort analysis in order to better

understand about societal change over the past two decades and how secular changes in the policy environment impacts on outcomes for individuals.

The Singapore Longitudinal and Life Course Cohort (SLLCC) is meant to be an opportunity to potentiate life course obesity research by offering the largest longitudinal cohort of youth (ages 7 to 18) in Singapore to-date. It consists of an extensive individual-level dataset of repeatedly measured anthropometric data, from about 2.7 million students born between 1973 to 2003, collected through routine annual school-based health screening in Singapore from 1990 to 2011.

By developing a secure platform in which routinely collected administrative data, existing cohort baseline and outcome data can be linked through the unique individual national identity card number, the research community and government bodies may enhance the understanding of anthropometric developments of children and adolescents in Singapore and its effects across the life course. The next steps after introducing the SLLCC cohort are to identify a range of research gaps and methodological challenges in determining the long-term effects of growth change on later health, thereafter, leading to the potential applications of the SLLCC dataset on childhood and adolescent growth.



## **Chapter 5: Anthropometric change over time in Singapore youth from 1990 to 2011**

### **Synopsis**

Now that the data preparation and epidemiological profile of the SLLCC has been fully described in Chapter Three and Four, it will be useful to address basic research questions next: Why do some individuals maintain a high or low BMI level throughout childhood and what explains why some individuals change more or less than others, as they grow older? What happens over time? Is growth or BMI change linear? These will be addressed in this Chapter Five, which explores secular trends through age, period and cohort (APC) analytical approaches to evaluate the impact of these effects on obesity trends among school-age children in Singapore. In addition, I will explore whether there is also a possible levelling of the obesity situation in Singapore and whether these trends differ between boys and girls, given emerging evidence on adolescents in western populations that the prevalence of obesity might have reached a plateau in the recent years (4-6).

Briefly, in this Chapter Five, the Zivot-Andrews Unit Root test (182) will be used to determine a break in trend of obesity prevalence based on annual time series data in SLLCC. On identification of the break-in-trend year, piecewise linear regression will be conducted to determine obesity trends in boys and girls before and after that particular year, separately for ages 6 to 12 and ages 13 to 18 so as to determine possible levelling of growth patterns during childhood and adolescent periods. Graphical representations (183) and use of the Median Polish Approach (184) will be conducted to evaluate age, period and cohort (APC) effects on obesity trends in school-age children in Singapore.

## 5.1 Introduction

Global reviews of the national prevalence of obesity and overweight among pre-school and school age children in the past five decades have consistently reported a rapidly increasing secular trend in most countries of the world (185, 186). From the 1970s to the end of the 1990s, the prevalence of overweight or obesity in school-age children doubled or tripled in several large countries in most regions, such as Canada and the United States in North America; Brazil and Chile in South America; Australia and Japan in the Western Pacific region, and Finland, Germany, Greece, Spain and the UK in Europe (185). In 2010, it was estimated that there were about 43 million overweight and obese preschool children (i.e. 2 standard deviations (SD) above the median WHO standards) in developing and developed countries. In addition, 92 million preschool children were estimated to be at risk of overweight (185). Although the prevalence of overweight and obesity in developed countries is about double that in developing countries (11.7% and 6.1%, respectively), the vast majority of affected children (35 million) live in developing countries. In addition, the relative increase in the past two decades has been higher in developing countries (+65%) than in developed countries (+48%) (185). The percentage of overweight children is highest in Latin America and the Caribbean (4.4%), followed by Africa (3.9%) and Asia (2.9%). However, in absolute numbers, Asia has the highest numbers of overweight children; 60% (or 10.6 million) of the overweight children from developing countries live in this region (186).

Obesity takes time to develop and excess weight takes time to be lost. The risks of becoming obese later in life start as early as the age of 5 years in elementary school (39). Accumulating evidence points to the detrimental effects of high BMI in childhood and early

adulthood on later life disease morbidity and mortality (38). Given the likelihood of persistence of overweight during childhood and adolescent (55) and the tracking of two key modifiable behaviours, food consumption and physical activity into adulthood (63), it is not surprising that mean adult BMI worldwide has increased by 0.4 kg/m<sup>2</sup> per decade (CI: 0.2–0.6) for men and 0.5 kg/m<sup>2</sup> per decade (CI: 0.3–0.7) for women between 1980 to 2008 (1). From a public health perspective, this is alarming given the risk of all-cause mortality for middle-aged adults with obesity (BMI  $\geq$  30kg/m<sup>2</sup>) could be 22% higher than those with normal weight (BMI 18.5–24.9kg/m<sup>2</sup>) (3).

Converging global evidence explaining the increasing numbers of people who are overweight and obese include the over-consumption of food, coupled with lives that are increasingly sedentary. At the same time, these factors are influenced by the rate in which countries progress along the demographic, nutritional and epidemiological transition (187, 188).

Since gaining independence in 1965, Singapore has completed the demographic transition with the ageing of our population primarily motivated by a fertility decline beginning in the 1970s (189). By 1976, the infant mortality rate (IMR) had been reduced to 11.8 and the neonatal mortality rate to 8.4. Singapore had the 6th lowest infant mortality rate in the world but only half the number of doctors in the 14 countries with the lowest IMR. The achievement was attributed to multiple factors impinging on the child: family planning, better nutrition, more paediatricians, better housing and increased gross national product (190).

It is also known that over the past half century, the availability of food has increased across the world and across regions. Diets have changed correspondingly, with increased consumption of food energy, above all from animal foods, fat and sugar. Rising incomes appear to be a prime driver of national diets, so much so that the concept of a dietary transition is taken as template for what may be expected as countries develop, with higher incomes, more urban living and more sedentary lives (188). In terms of the nutritional transition in Singapore, we have also entered the last phase of nutritional transition with the shift of nutritional intake from relatively monotonous diets of varying nutritional quality, based on locally grown vegetables and fruits, and limited food of animal origin to increases in the consumption of animal-sourced food and “fast food” (191). Although the adult Singaporean’s diet met the minimum recommendations for various macronutrients and micronutrients, the findings of the 2004 National Nutrition Survey indicated areas of concerns such as the excessive intake of energy, total fat, saturated fat and cholesterol which were above and beyond the recommendations (more than 100% of recommended intake). Compared with 1998, more adult Singaporeans in 2004 had excessive intakes of energy, total fat, saturated fat and cholesterol (192). This was very much in-line with both regional (187) and global trends among rapidly rising economies such as China (188).

The epidemiological transition leading to higher prevalence of non-communicable diseases associated with overweight and obesity is evident from the increasing trends observed in prevalence of Type II diabetes and hypercholesterolemia in Singapore (21). These shifts are largely associated with behavioural changes in dietary profile and lifestyle and decreased indulgence in physical activity (21).

## 5.2 The obesity plateau phenomena

An emerging set of studies on adolescents in western populations had shown that the prevalence of obesity might have reached a plateau in recent years (4-6). The prevalence of overweight and obesity was 31.7% and 16.9% in 2007–2008 in North American children and adolescents aged 2–19 years, with no statistically significant trends noticed over the time periods of 1999–2000 until 2010 (6, 193). A recent study from Sweden also reported stabilisation of trends in prevalence of childhood overweight and obesity from 1999 to 2005 (5).

Similar findings have been reported in separate investigations of the levelling off of the epidemic in children and adolescent from Australia, Europe, Japan and the USA (194). In Europe, a stabilisation (195-200), a levelling off or a decrease in the prevalence of obesity was observed in several countries, except for Germany where a slight increase was found in boys and girls (201). Stability in the prevalence was also found in Russian boys and girls (202). In Asia, a decrease in the prevalence was observed in Japanese boys and girls (203), whereas a continuously strong increasing trend was still evident in Chinese and Vietnamese children (204), (205). In Australian boys and girls, the obesity prevalence was stable (206). In the USA, five studies have shown either stability or a levelling off in the prevalence of obesity in both boys and girls (4, 6, 207-209). Of the studies that reported a change in the obesity trend, the turning point seemed to occur predominantly in the early 2000s.

Until now, there has not yet been an attempt to elucidate the possibility of a levelling of obesity situation in Singapore.

### 5.3 Singapore anthropometric studies

In the last five decades, there have been four major growth studies reported for pre-school and four studies on school-age Singapore children from 1957 to 2002. Anthropometric growth monitoring was first reported in 1954 on the nutritional status of Malay, Chinese and Indian infants and pre-school children. However, detailed data from these studies were not available for comparison with the current PhD data. A subsequent review of the anthropometric trends noted that the mean heights of pre-school and school-age boys and girls had significantly increased from 1975 till 1993, but had not increased significantly from 1993 as compared to the most recent study in 2002. Authors suggested that the present heights of school age Singapore children had probably reached their optimal genetic potential, as a consequence of significantly improved living standards; better nutrition and better medical care for children. However, the weights of boys continued to increase significantly from 1975 through to 2002, a trend which was also seen in school-age girls (210).

A large review of annualised changes in prevalence levels of obesity and overweight in school-age children across 60 countries (out of 191 WHO member countries) has found that virtually all (58 out of 60) countries had recorded an increasing prevalence from 1980 to 2005, where data were available (186). This secular trend was observed regardless of the use of International Task Force on Childhood Obesity (IOTF) classifications or national/local classifications. Reports on the situation in Singapore highlighted an overweight prevalence rate of 0.5% among pre-schoolers (aged 0 to 5.99) from 1970 to 1977, based on a national sample of 9,655. It was not surprising that significant wasting or low weight-for-height in children (almost 5%) was the greater challenge observed in the first five years of gaining independence post-1965

in Singapore (186). Whereas among school age children in 1976, the prevalence of obesity (defined as body weight more than 120% of the standard weight-for-height) was only 1.4% for Primary 1, and it had increased 9-fold to 12.7% by 2006. Similarly, the obesity prevalence was 2.2% in Primary 6 students 30 years ago, and it increased 7-fold to 15.9% in 2006 (210). These findings were consistent to some extent with a 1994 study, which concluded generally that pre-school children in Singapore have grown taller, heavier and have larger head circumference when compared to their counterparts more than 15 years previously (from 1972-75 to 1987-8) (211).

The prevalence of obesity has declined from 16.6% to 14.6% between 1992 and 2000 among primary 6 students (11 to 12 year olds) with some researchers proposing that this may be due to the implementation of school-based interventions in Singapore in the early 80s (81). A similar decline has been seen in secondary 4 students (15 to 16 year olds) from 15.5% to 13.1% over the same period (81). However, within the last decade, amongst school children, based on BMI-for-age norms, there has been an increase in the percentage of overweight children at school entry age from the year 2000 (6.5%) to 2006 (7.8%). This had been followed by a slight decrease from 2007 (7.6%) to 2010 (7.4%). The percentage of overweight students also increased from Primary 1 to Primary 5/6, for both female and male students. However, the percentage of overweight children among Primary 6 students decreased from 2008 to 2010, from 10.8% to 10.2% (82).

The nationally representative studies in Singapore are often cross-sectional surveys. When data were collected from a large number of individuals, it did not necessarily include

many individuals at every age. To date, Singaporean longitudinal anthropometric studies among pre-school and school-age are limited (162, 163). These prospective cohorts are based on selective pooling of various cross-sectional national surveys, in which respective participants, mostly adults, were contacted for subsequent follow-up health screening or monitoring of particular chronic conditions (155, 159, 160, 212, 213).

An indirect approach to studying growth over time would be to extract anthropometric measurements from these cohorts, even though they had different clinical objectives in mind when they were established. A disadvantage is that these cohorts are either small with a limited number of children or adolescents studied, or they do not have that many measurements per individual over time. Also, the data in many of these studies were specifically collected for research purposes, and the age when the children were to be measured may not be the same across studies, thus limiting analysis of growth patterns within the same age groups.

#### **5.4 Classification of obesity and overweight**

In adults, there is a consensus on the definition of overweight and obesity, whereas there is no agreed definition on child and adolescent overweight and obesity (214). Body mass index (BMI) at or above 25 kg/m<sup>2</sup> denotes overweight in adults. BMI at or above 30 kg/m<sup>2</sup> are classified as adult obesity (215). In children, BMI increases from birth until 1 y of age and then decreases until 5–9 years of age. The age at which the BMI begins to increase is the so-called adiposity rebound. Therefore, it is necessary to have age- and gender-specific cut offs of BMI for children and adolescents up to the age of 17 year old.



To overcome this problem, the International Task Force on Childhood Obesity (IOTF) have published age- and gender-specific cut offs of BMI (216). The cut offs are based on measured height and weight in children from two European countries (UK and the Netherlands), two Asian (Hong Kong and Singapore), Brazil, and The United States in previously conducted surveys (216). The IOTF method assumed that the data followed a normal distribution. In practice, the distribution of BMI is skewed with a longer tail above the mean than below, and thereafter, estimated prevalence rates are thus likely to be lower than the true prevalence rates (217).

In 2006, the World Health Organization (WHO) launched new growth standards for children irrespective of ethnicity, socio-economic status and feeding mode (218). The WHO Child Growth Standards were based on the WHO Multicentre Growth Reference Study (MGRS), which was implemented between 1997 and 2003 to develop growth standards for children below 5 years of age. The MGRS collected primary growth data and related information from 8,440 healthy breastfed infants and young children from diverse ethnic backgrounds and cultural settings (219).

By April 2011, at least 125 countries, representing 75% of the world's under-5 population, had adopted the standards and were at varying stages of their implementation (170). It is important to note that WHO standards depict how children should grow, on average, in all countries, when properly fed and cared for, rather than merely describing how they grew at a particular time and place (170).

Routine growth monitoring of children in Singapore has been a priority for the Ministry of Health since the early 1970s. From 1970 to 1973, nutritional assessment was based on national growth charts of Singapore children and obesity was defined as greater than or equal to 120% of the standard. From 1981 onwards, five weight-for-height cut offs were created: C < 80% of standard; B/C  $\geq$  80% < 90% of standard; A  $\geq$  90% < 110% of standard; B/O  $\geq$  110% < 120% of standard and O  $\geq$  120% of standard. The standards were subsequently changed to Harvard weight-for-height tables, despite potential errors arising through using the Harvard tables and percentage levels of median weight-for-age in assessing nutritional status (220). From 1984 onwards, anthropometric assessments were updated to the 1983 Singapore standard weight-for-height tables compiled by School Health Services, Singapore. In addition, percentile charts derived from a cross-sectional anthropometric study of 13,565 children aged 0-6 years old in 1988 were also in use in place of the NCHS/CDC/WHO's curves for growth monitoring and screening purposes in Singapore (211).

## **5.2 Aim of this new study**

The aim of this new study is to utilise a large population school-based data set of routinely collected anthropometric data from 1997 to 2011 to address the following questions:

1. Is there a possible levelling of obesity trends in Singapore and do trends differ for boys and girls?
2. What are the age, period and cohort effects influencing obesity trends among school-age children in Singapore?
3. Is there a difference between estimates of the extent of obesity in school-age children in Singapore from 1997 to 2011 when using international BMI age- and gender-specific cut offs

based on WHO Child Growth Standards, compared to the existing practice of using nutritional status?

## **5.3 Methods**

### **5.3.1 Data sets**

Anthropometric trends were explored using data from the Ministry of Education's school-based "Trim and Fit" programme and hand searching of Annual School Health Reports compiled by the Singapore Health Promotion Board.

#### ***5.3.1.1 Trim and Fit, 1997-2011***

Briefly, in 1992, Singapore's health ministry launched a national programme promoting a healthy lifestyle to address the common risk factors for chronic diseases such as obesity, physical inactivity, and cigarette smoking. Different age groups in the population were targeted, including school children. The Health Promotion Board (HPB) of the Ministry of Health (MOH) works in close partnership with the Ministry of Education (MOE) on obesity programmes for school children. The MOE's "Trim and Fit" (TAF) programme for primary, secondary, and pre-university schools aimed to reduce obesity in school children and improve the physical fitness of the pupils using a multi-disciplinary approach targeting overweight students, parents, teachers, and the school environment. Under the programme, schools were recognised for their efforts in improving physical fitness and reducing obesity in their schools. Each year, schools were banded according to their fitness index and results in the National Physical Fitness Award (NAPFA) test and percentage of overweight students.

The height and weight of almost all Primary and Secondary school students who had to undergo the compulsory NAPFA test were measured by a physical education teacher using standard weighing and height machines. These anthropometric data were recorded and submitted to the MOE as part of the on-going monitoring of physical fitness and health screening under the TAF Program.

For the purposes of this study, annual records of TAF from 1997 to 2011 were provided to an external third party data vendor to be de-identified by replacing the students' NRIC numbers with a unique record identifier string number. In addition, individual demographic data on gender, race, postal code of residence, date of birth, school code and educational level were added to each student record. Annually, an average of 500,000 students in 203 primary schools and 172 secondary schools were compiled in the TAF dataset.

### ***5.3.1.2 Annual School Health Reports, 1974-2010***

Every year, the School Health Service (SHS) of the Health Promotion Board in Singapore conducts routine health screening for school children in all primary schools (for ages 6 to 12) and 95% of all secondary schools (for ages 13 to 16) in Singapore. The reader is referred to Chapter Three for more details on SHS and its datasets.

At the end of each academic year, an annual School Health Report describing the nutritional status and body weight classification of students screened by the SHS was compiled. Relevant anthropometric data was extracted from hard copies of the reports from 1974 to 2010 for this study.

### **5.3.2 Investigation of possible levelling of obesity trends**

Mean percentage obesity in boys and girls across all ages, ages 6-12 and 13-18 were examined to see whether growth trends were different between primary schooling and secondary schooling periods from 1997 to 2011. Visual inspection of the trend was complemented by the use of the Zivot-Andrews Unit Root test to statistically determine a structural break in trend of time series data (182). On identification of the break-in-trend year, piecewise linear regression was conducted for obesity trends in boys and girls before and after that particular year, separately for ages 6 to 12 and ages 13 to 18 so as to determine possible levelling of growth patterns in during childhood and adolescent periods. A sensitivity analysis was also conducted to determine whether the break-trend year would differ if the tests were ran to detect a breakpoint based on intercept only.

### **5.3.3 Age, period, cohort effects**

Graphical representations (183) and use of the median polish approach (184, 221, 222) were conducted to evaluate age, period and cohort (APC) effects on obesity trends in school-age children in Singapore.

#### **Graphical representation methods:**

1. The weight status classification of students in 2-year age groups was compared within the cross-sectional health screening at schools, disaggregated by gender and ethnic race groups.

2. The mean percentage obesity, overweight, normal weight, Grade 1, 2 and 3 Thinness at each age was compared across selected periods (1997, 1999, 2001, 2003, 2005, 2007, 2009 and 2011).
3. Period trends in % obese among ethnic youth (ages 6 to 18) in Singapore were compared across time and age separately, and
4. Different mean percentage weight classifications within different cohorts (subjects born in 1983 to 2003) were followed over time using longitudinal data.

### **Median polish method:**

This approach explicitly tested whether the effect of age and period interacted to produce a cohort effect that was more than what would be expected given their additive influences.

Median polish analysis relied on the use of a contingency table with obesity prevalence stratified by m age groups in rows and n period in columns. The median polish approach removed the additive effect of age (row) and period (column) by iteratively subtracting the median value of each row and column. After several iterations, the residual values stabilised (the median residual of each row or column approximates zero). These residuals were then regressed on indicator variables for cohort membership using standard linear regression; the extent to which the cohort variable predicted the residual was the cohort effect. The remaining residual unaccounted for by cohort was considered to be non-systematic random error (223).

Graphical trend analyses and the contingency table used in the median polish analysis were done using basic Microsoft Office 2011 Excel spread sheet software. Simple regression analysis were done using Stata version 12.0 (149).

### 5.3.4 Difference in classification of obesity

Percentage obesity (BMI-for-age) among school-age children, both girls and boys was determined and compared using age-specific child and adolescent international BMI cut offs ( $>30\text{kg/m}^2$  at 18 years) and nutritional status ( $>120\%$  of standard) from 1997 to 2011. Sex-specific BMI-for-age z-scores were standardised for all students, using the Stata command “zanthro” (172), derived from WHO child growth standards so that results can be internationally more comparable.

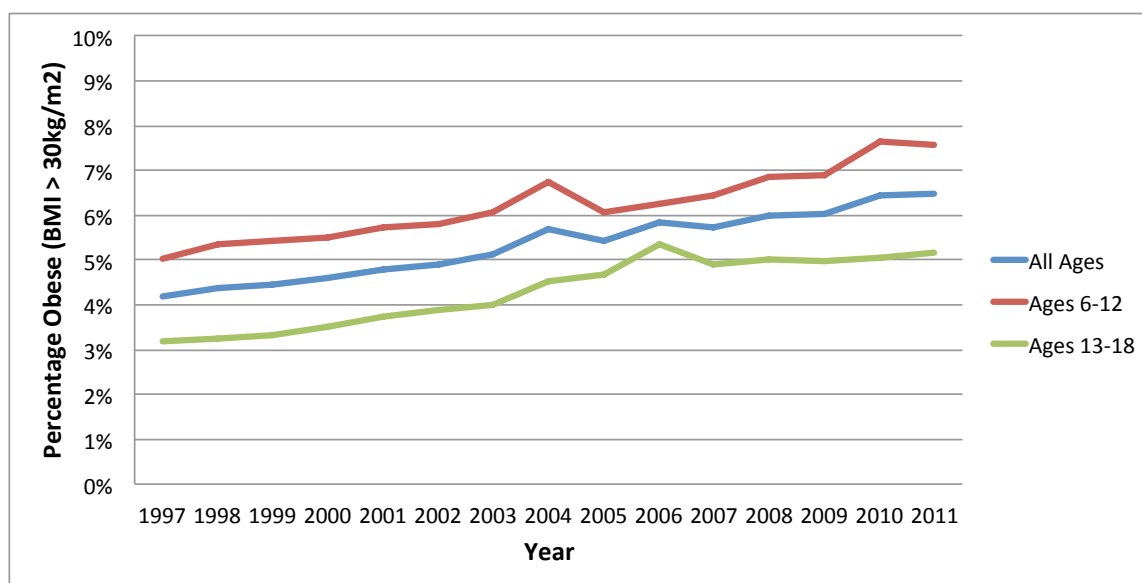
## 5.4 Results

### 5.4.1 Possible levelling of obesity situation

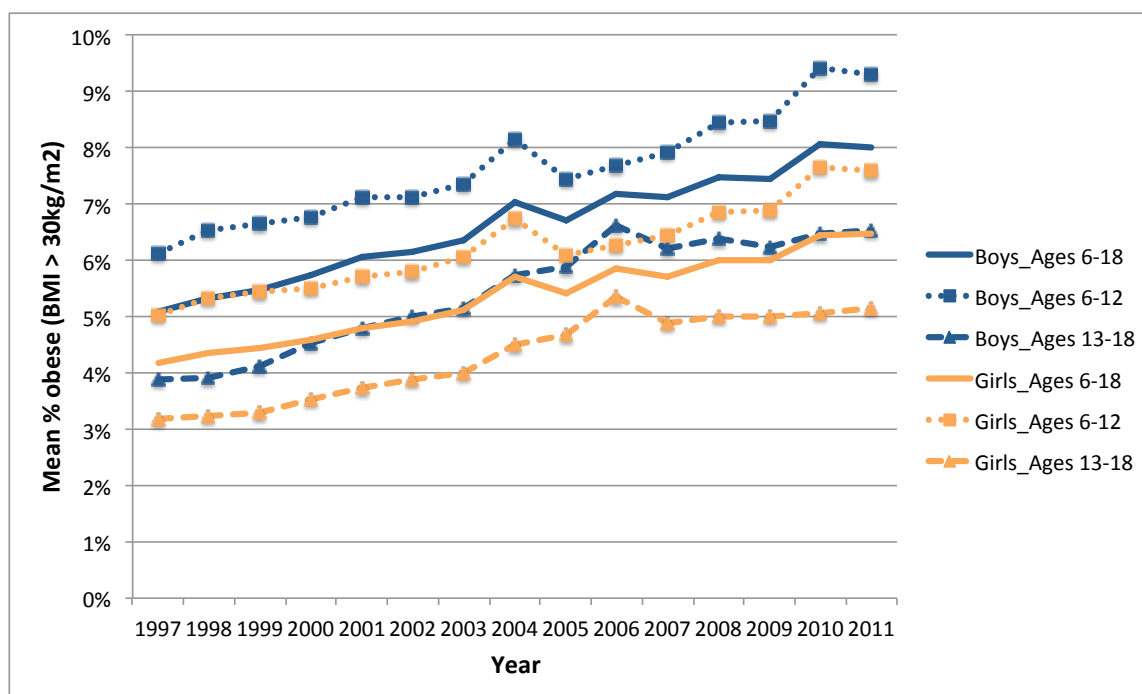
Visual inspection of mean annual (1997-2011) percentage obesity trends among school-age children ages 6 to 18 suggested that in both boys and girls, there might be a possible levelling of the obesity situation after 2006 (Figure 4 and Figure 5). Piecewise linear regression of annual percentage obesity trends in school-age children in Singapore confirmed that there was a plateau in obesity from 2008 to 2011 in both boys and girls (age 13 to 18). This effect was slightly more pronounced for girls than for boys (Table 37). The Zivot-Andrews Unit Root test (using Stata command: ZANDREWS) located a single breakpoint on both intercept and trend breaks in the year 2008. Between 1997 to 2008, the prevalence of obesity increased linearly in both boys between ages 6 to 12 (rate of change at 95% confidence interval was 0.17, CI: 0.12–0.23) and girls (rate = 0.11, CI: 0.07–0.15) (Figure 6) with the steepest increase seen in boys aged 13 to 18 (rate = 0.28, CI: 0.24–0.32) and in girls (rate = 0.15, CI: 0.10–0.20) (Figure 7).

A sensitivity analysis was conducted to determine if the break-trend year would differ if the tests were set to detect a breakpoint based on intercept. Testing results (not shown) found that if only

a break in intercept is defined, then the levelling of obesity for boys and girls aged 13 to 18 would have been detected earlier in 2007 and later for girls aged 6 to 12 in 2009.

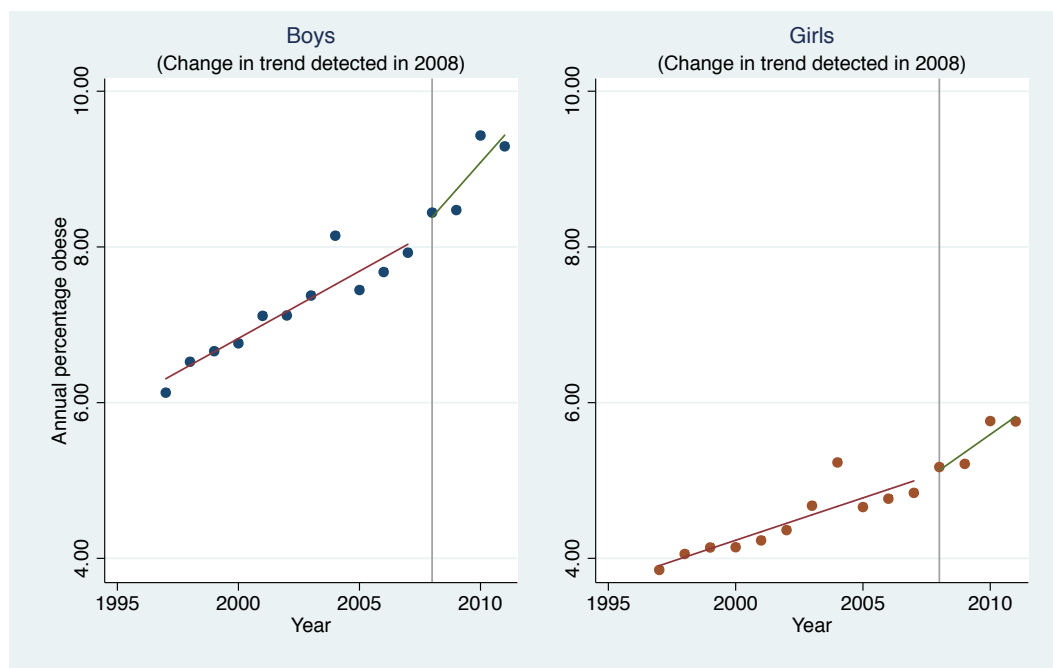


**Figure 4 Mean annual percentage obese among children ages 6 to 18 from 1997 to 2011 in Singapore**

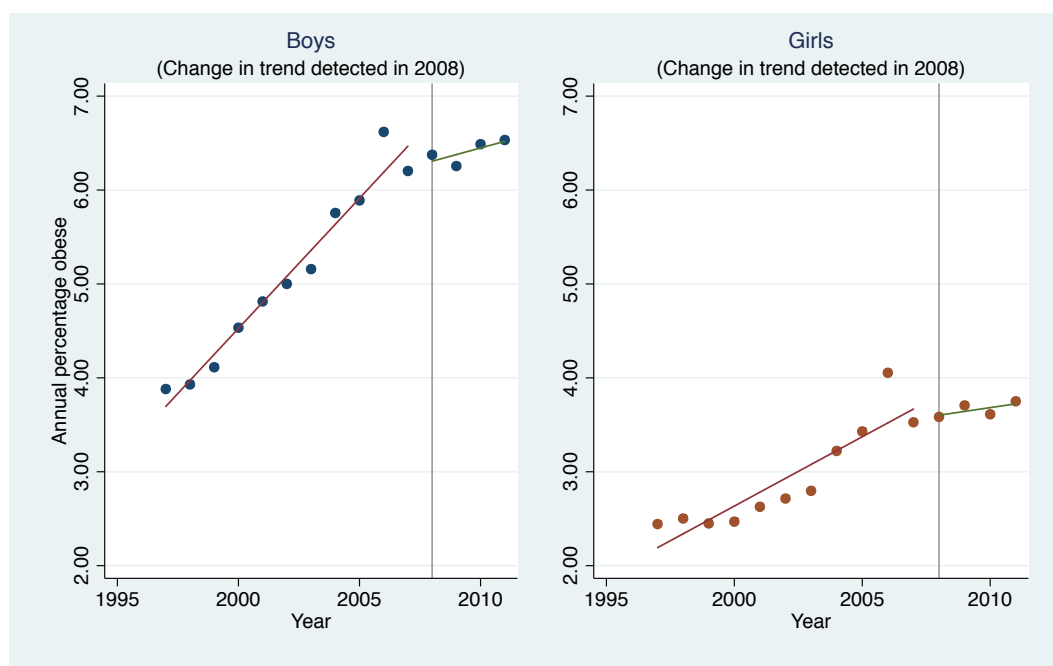


**Figure 5 Differences in mean annual percentage obese between boys and girls aged 6 to 18 from 1997 to 2011 in Singapore**





**Figure 6 Obesity trends in boys and girls aged 6 to 12 in Singapore from 1997 to 2011**



**Figure 7 Obesity trends in boys and girls aged 13 to 18 in Singapore from 1997 to 2011**

**Table 37 Piecewise linear regression of obesity trends in children aged 6 to 18 in Singapore from 1997 to 2011 (with change in trend detected in 2008)**

	Coefficient	95% Confidence Interval		P-value
Obese Boys (age 6-12)				
Intercept 1	8.21	7.83	8.58	<0.01
Intercept 2	8.38	7.90	8.87	<0.01
Slope 1	0.17	0.12	0.23	<0.01
Slope 2	0.35	0.09	0.61	0.01
Obese Boys (age 13-18)				
Intercept 1	6.74	6.48	7.01	<0.01
Intercept 2	6.31	5.96	6.65	<0.01
Slope 1	0.28	0.24	0.32	<0.01
Slope 2	0.07	-0.12	0.26	0.42
Obese Girls (age 6-12)				
Intercept 1	5.10	4.81	5.40	<0.01
Intercept 2	5.13	4.75	5.51	<0.01
Slope 1	0.11	0.07	0.15	<0.01
Slope 2	0.23	0.03	0.43	0.03
Obese Girls (age 13-18)				
Intercept 1	3.82	3.49	4.14	<0.01
Intercept 2	3.60	3.18	4.03	<0.01
Slope 1	0.15	0.10	0.20	<0.01
Slope 2	0.04	-0.19	0.27	0.70

## 5.4.2 Age, period, cohort effects

### 5.4.2.1 Graphical representations

In 1997, 11.6% of the children and adolescent aged 6 to 18 on average were classified as overweight (equivalent to BMI 25 to <30kg/m<sup>2</sup> at 18 years old) using international sex-specific BMI-for-age cut-offs. 4.2% were considered obese (equivalent to BMI >30kg/m<sup>2</sup> at 18 years old). Overall, 21.3% of the cohort was under-weight (equivalent to BMI <18kg/m<sup>2</sup> at 18 years old) with those at ages 6-7 and 17-18 being most affected. See Table 38 for general demographic characteristics and weight profile of school-age student population in 1997.

**Table 38 Demography and weight profile of school-age children in Singapore in 1997**

	6-7 year old		8-9 year old		10-11 year old		12-13 year old		14-15 year old		16-18 year old	
<b>Age at baseline</b>	<b>Male</b>	<b>Female</b>	<b>Male</b>	<b>Female</b>	<b>Male</b>	<b>Female</b>	<b>Male</b>	<b>Female</b>	<b>Male</b>	<b>Female</b>	<b>Male</b>	<b>Female</b>
<i>N</i>	39,622	36,935	50,375	47,177	40,871	37,752	41,070	37,792	40,142	37,160	31,455	29,737
<b>Weight classification <sup>a</sup></b>												
Grade 2 Thinness (%)	6.2	6.6	4.0	5.0	3.5	4.3	2.7	3.2	2.6	3.2	3.5	6.0
Grade 3 Thinness (%)	3.5	4.4	1.8	2.6	1.5	2.2	1.1	1.6	0.9	1.6	1.5	2.4
Grade 1 Thinness (%)	17.1	17.6	14.9	16.1	12.4	13.6	11.1	12.5	11.5	14.6	13.9	19.3
Normal weight (%)	57.6	58.9	56.4	59.7	57.8	61.6	63.4	67.3	67.5	70.6	68.3	64.9
Overweight (%)	9.9	8.7	16.0	12.4	18.6	14.4	16.7	12.0	13.0	7.5	9.4	5.3
Obese (%)	5.7	3.7%	6.9	4.1	6.3	3.9	5.0	3.3	4.4	2.6	3.4	2.3
<b>Ethnic race group</b>												
Chinese (%)	71.4	71.2	73.5	73.5	71.4	71.2	74.0	74.0	76.5	77.0	78.8	79.6
Malay (%)	13.1	13.2	12.1	11.9	13.0	13.1	11.8	11.6	10.4	10.2	9.0	8.2
Eurasian (%)	0.4	0.5	0.4	0.4	0.4	0.4	0.3	0.4	0.3	0.4	0.4	0.4
Indonesian (%)	6.0	5.8	5.6	5.4	5.9	5.8	5.4	5.4	4.9	4.7	4.3	4.0
Indian (%)	7.9	8.3	7.5	7.8	8.2	8.3	7.5	7.7	6.9	6.9	6.8	7.0
Other (%)	1.1	1.0	1.0	1.0	1.1	1.1	1.0	0.9	0.9	0.8	0.8	0.8

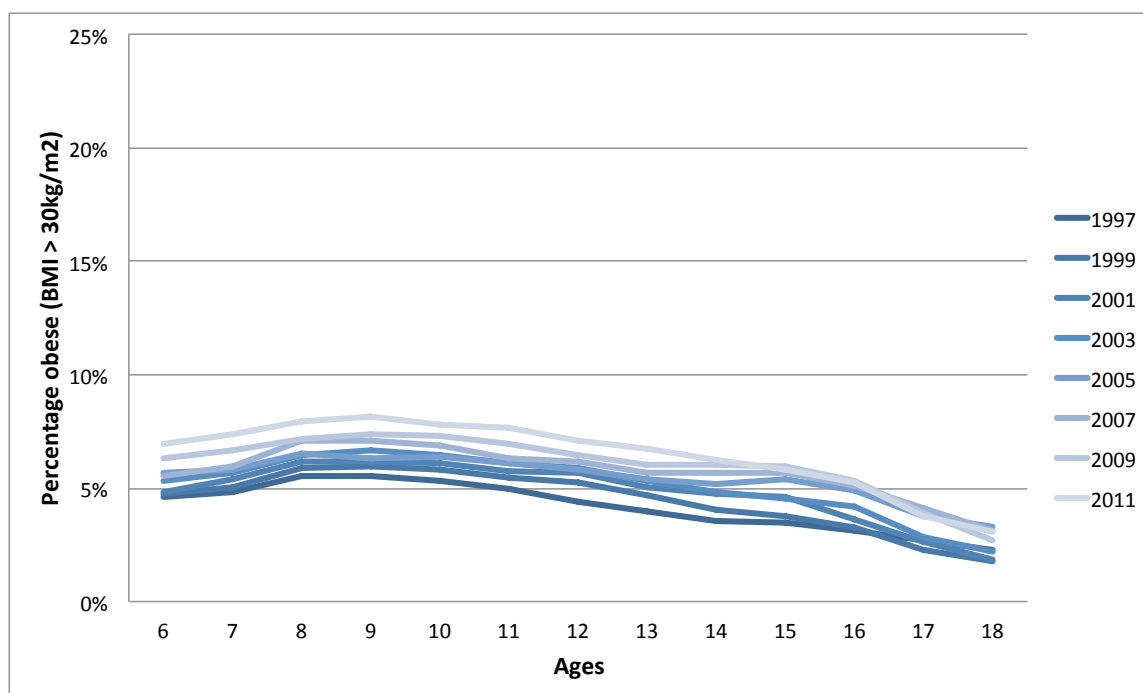
Notes:

<sup>a</sup> BMI range at 18 years: Obese (>30 kg/m<sup>2</sup>), Overweight (25 to 30 kg/m<sup>2</sup>), Normal (18.5 to 25 kg/m<sup>2</sup>), Grade 1 thinness (17 to 18.5 kg/m<sup>2</sup>), Grade 2 thinness (16 to 17 kg/m<sup>2</sup>), Grade 3 thinness (<16 kg/m<sup>2</sup>)

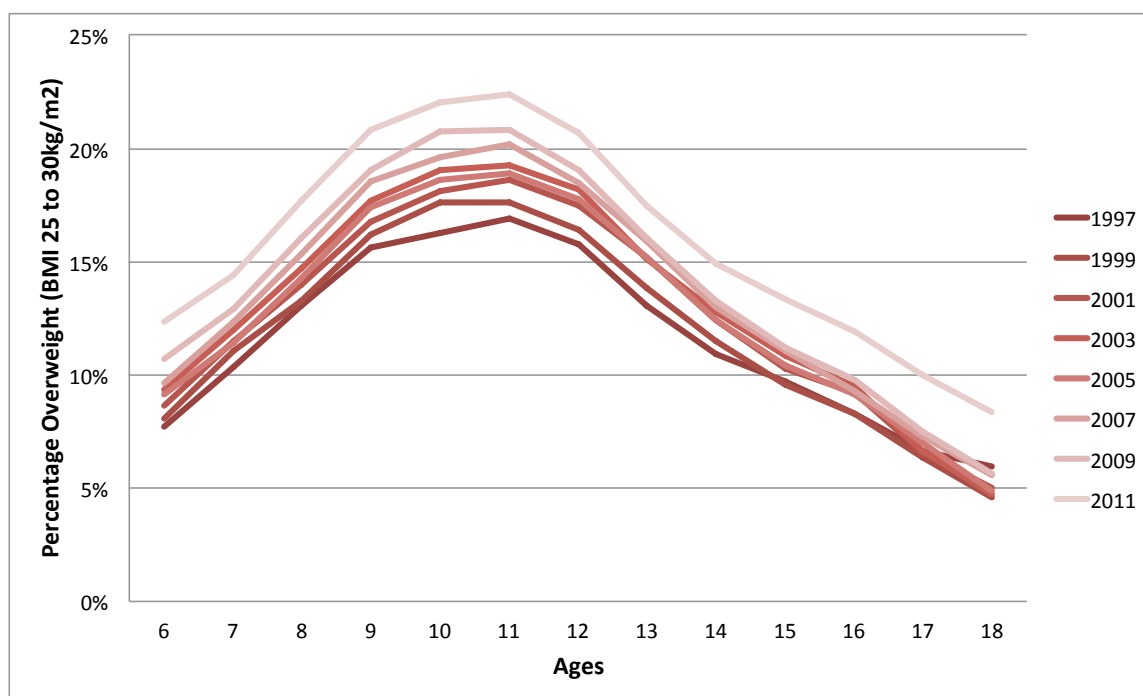
After 14 years, the prevalence of overweight and obesity were increased to 15.9% and 6.7% respectively in 2011. Higher prevalence of overweight were observed in boys than in girls across all age groups with the highest increase for boys between age 6 to 8 with a steady decline as they grew up. % Overweight trends for girls reached its peak at age 11 and tapered gradually to its lowest at age 18. The % Underweight status trends for both boys and girls from ages 6 to 18 were similar with the highest prevalence at 32.8% for girls at age 18 and 29.6% for boys at age 6.

Prevalence of overweight and obesity across all ages increased from older (year 1997 at baseline) to more recent periods. Boys and girls were most overweight between ages 9 to 12 with lower proportions overweight at age 6 and 18 (Figure 8 and Figure 9). Percentage of normal weight students did not differ significantly across years. Age-period trends were decreasing for all grades of thinness in chronological order with grade 2 (equivalent to BMI 16 to  $<17\text{kg/m}^2$  at 18 years old) and 3 (equivalent to BMI  $<16\text{kg/m}^2$  at 18 years old) showing greater decline at young ages (Figure 10, Figure 11 and Figure 12).

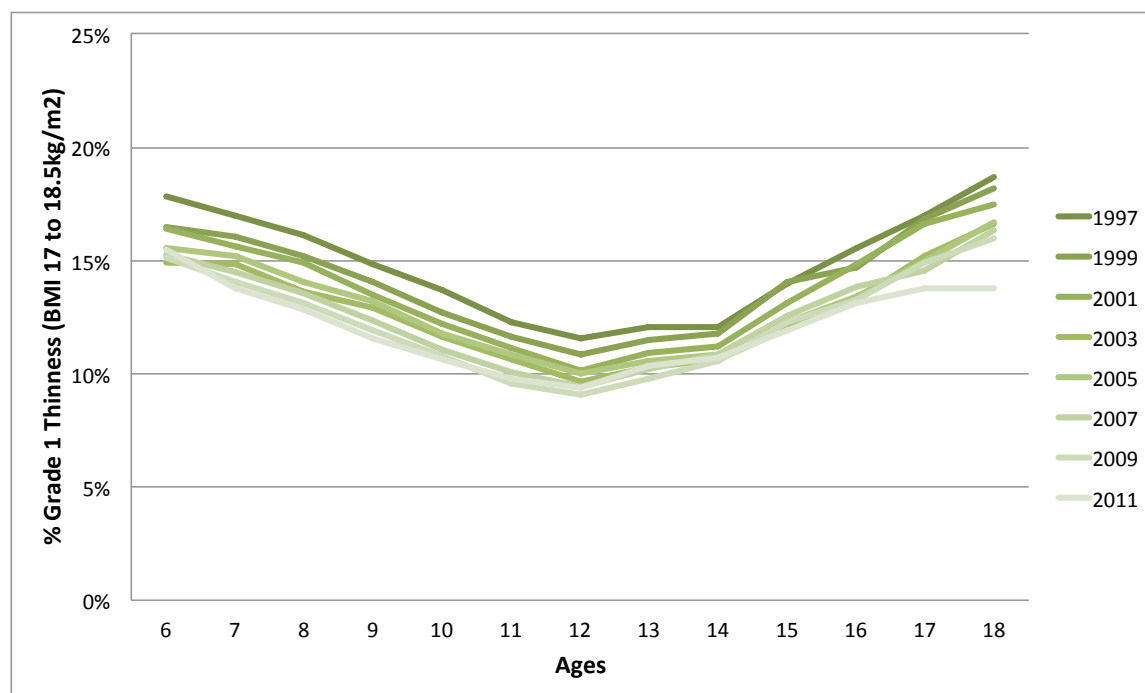
Period analysis of % obesity among ethnic youth (ages 6 to 18) showed an increasing trend with highest prevalence rates observed for Indonesians and Malays, followed by Indians, Eurasians and Chinese (Figure 13 and Figure 14).



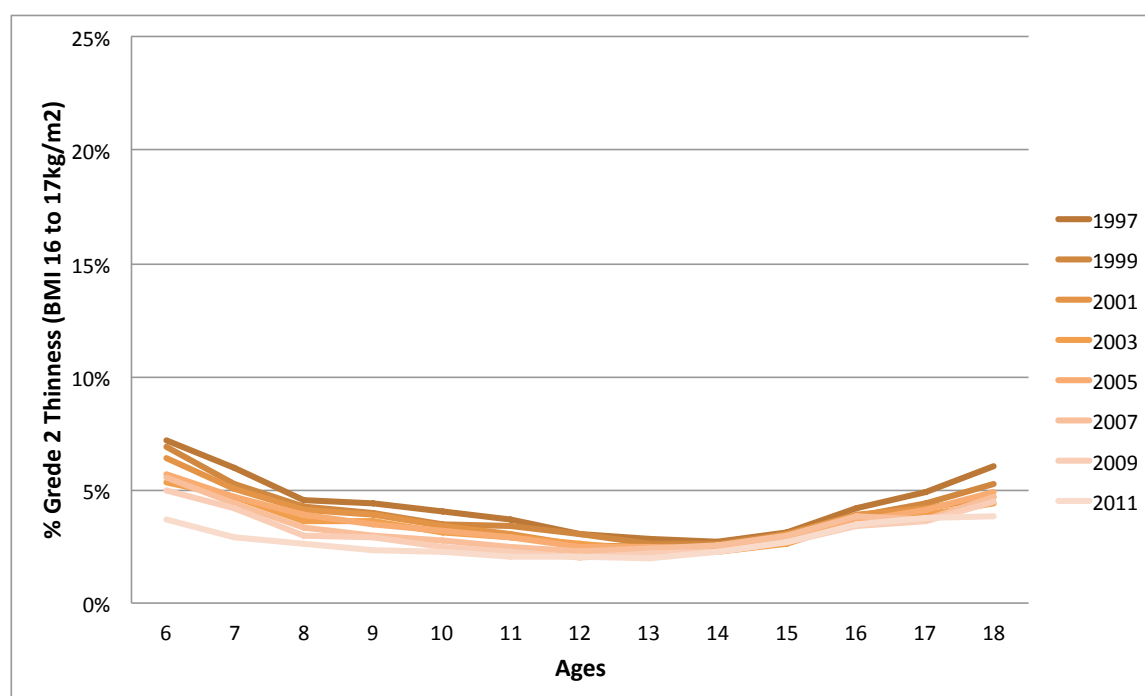
**Figure 8 Age-period obesity (BMI > 30kg/m<sup>2</sup>) trends among children aged 6 to 18 in Singapore from 1997 to 2011**



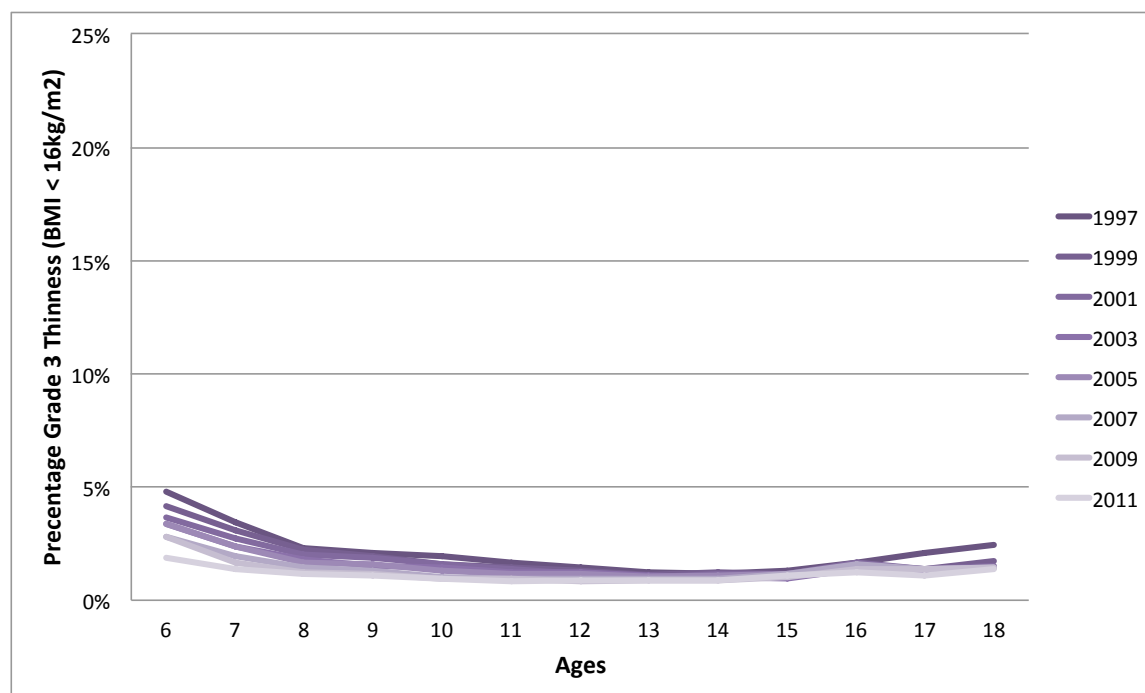
**Figure 9 Age-period overweight (BMI 25 to 30kg/m<sup>2</sup>) trends among children aged 6 to 18 in Singapore from 1997 to 2011**



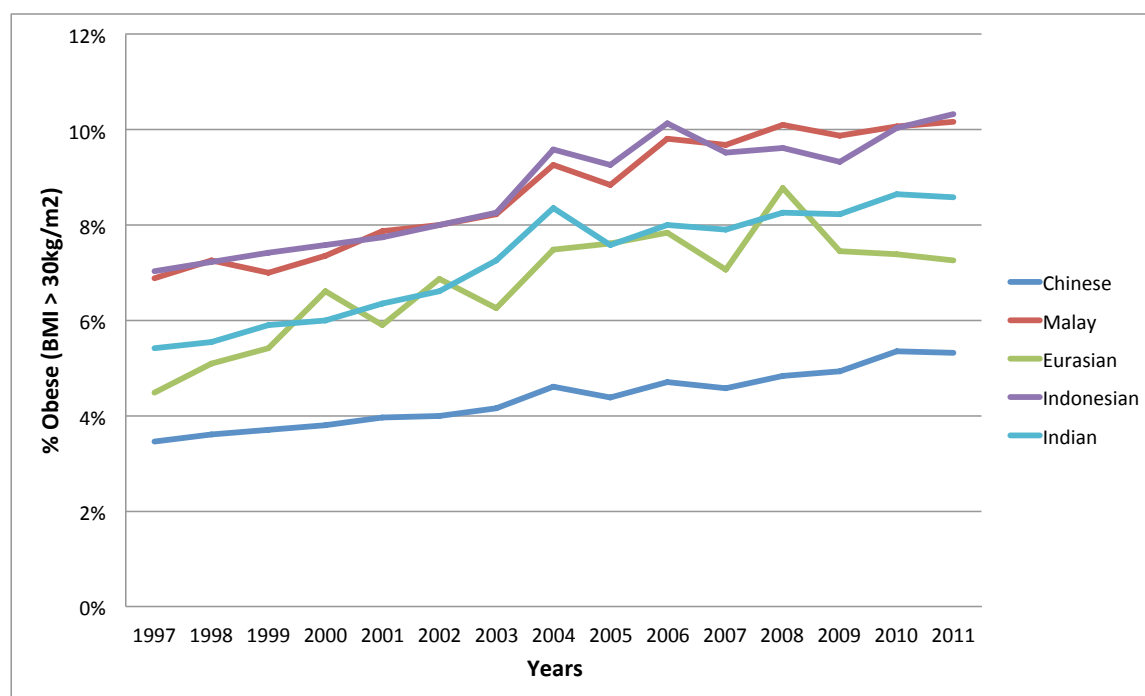
**Figure 10** Age-period grade 1 thinness (BMI 17 to 18.5kg/m<sup>2</sup>) trends among children aged 6 to 18 in Singapore from 1997 to 2011



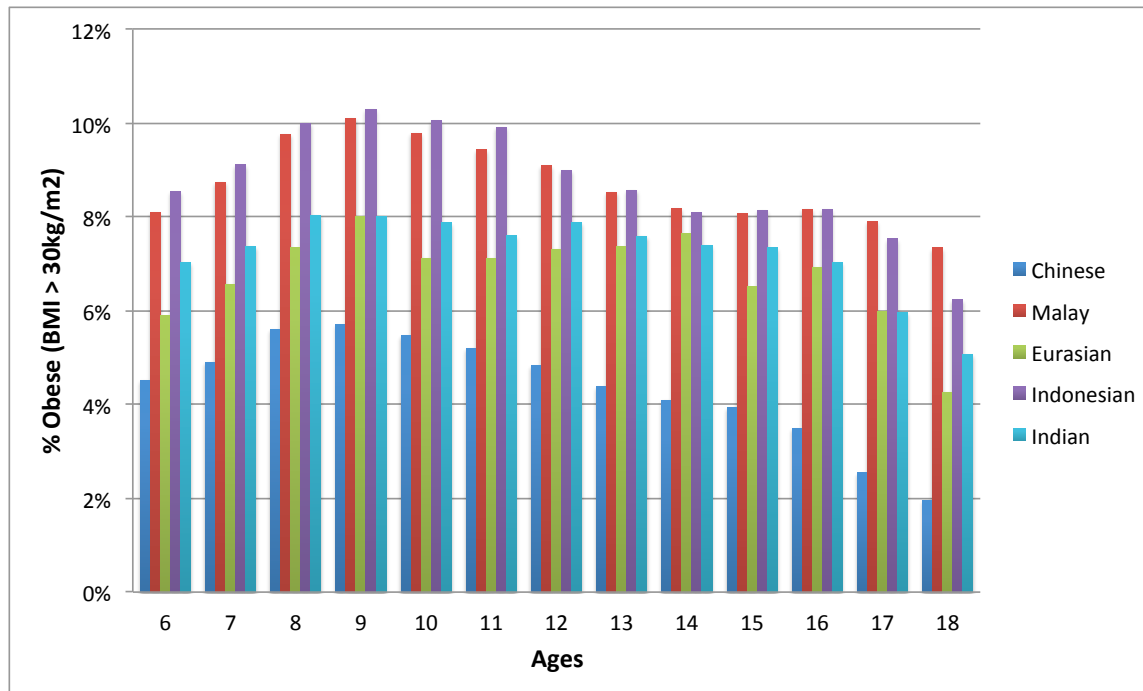
**Figure 11** Age-period grade 2 thinness (BMI 16 to 17kg/m<sup>2</sup>) trends among children aged 6 to 18 in Singapore from 1997 to 2011



**Figure 12 Age-period grade 3 thinness (BMI < 16kg/m<sup>2</sup>) trends among children aged 6 to 18 in Singapore from 1997 to 2011**



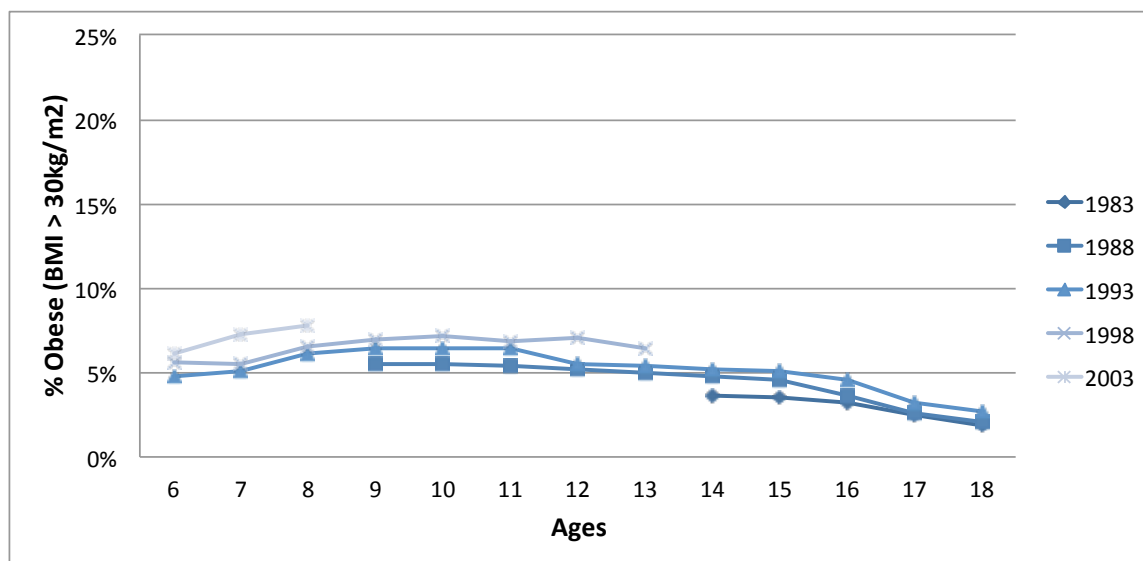
**Figure 13 Annual obesity trends (BMI > 30kg/m<sup>2</sup>) among children aged 6 to 18 by race groups in Singapore from 1997 to 2011**



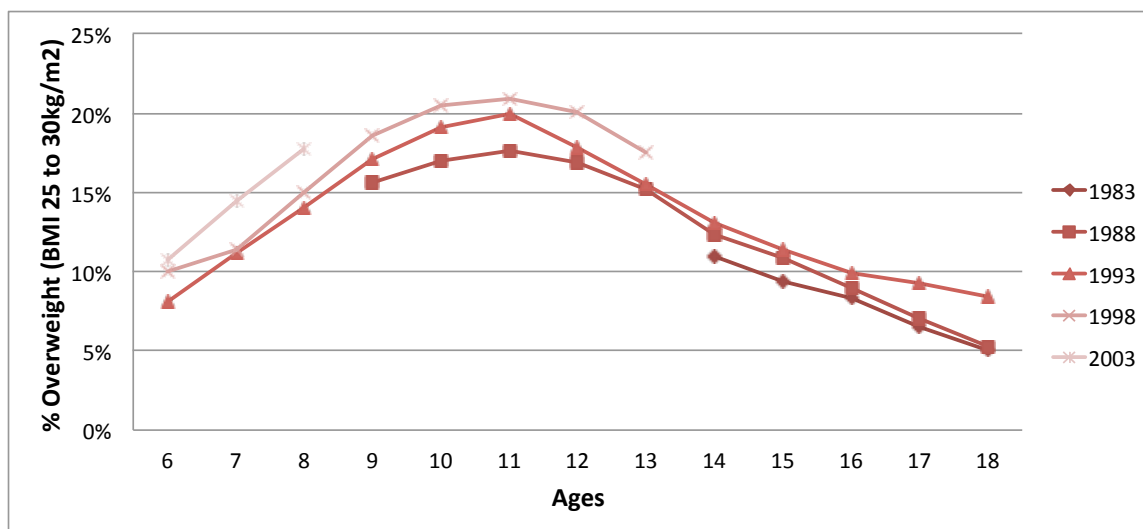
**Figure 14 Percentage obesity (BMI > 30kg/m<sup>2</sup>) of each race groups at ages 6 to 18 in Singapore from 1997 to 2011**

Youth born in later cohorts (2003) were presumed to have successively higher body weight than earlier-born cohorts (1983, 1988, 1993, 1998), based on the trends observed in cohort-stratified age trends of % obesity and overweight rates (Figure 15 and Figure 16). Normal weight prevalence remained relatively unchanged in all cohorts. Cohort trends in all grades of thinness reflected the opposite effect of being successively lower for more recent cohorts than for earlier-born cohorts (Figure 17, Figure 18 and Figure 19).

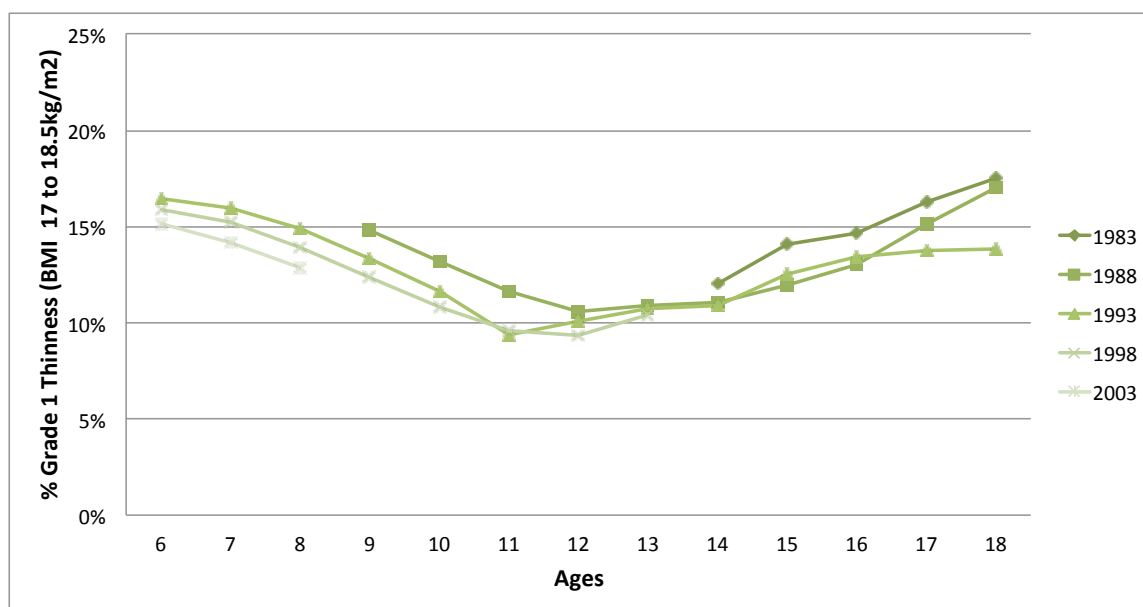




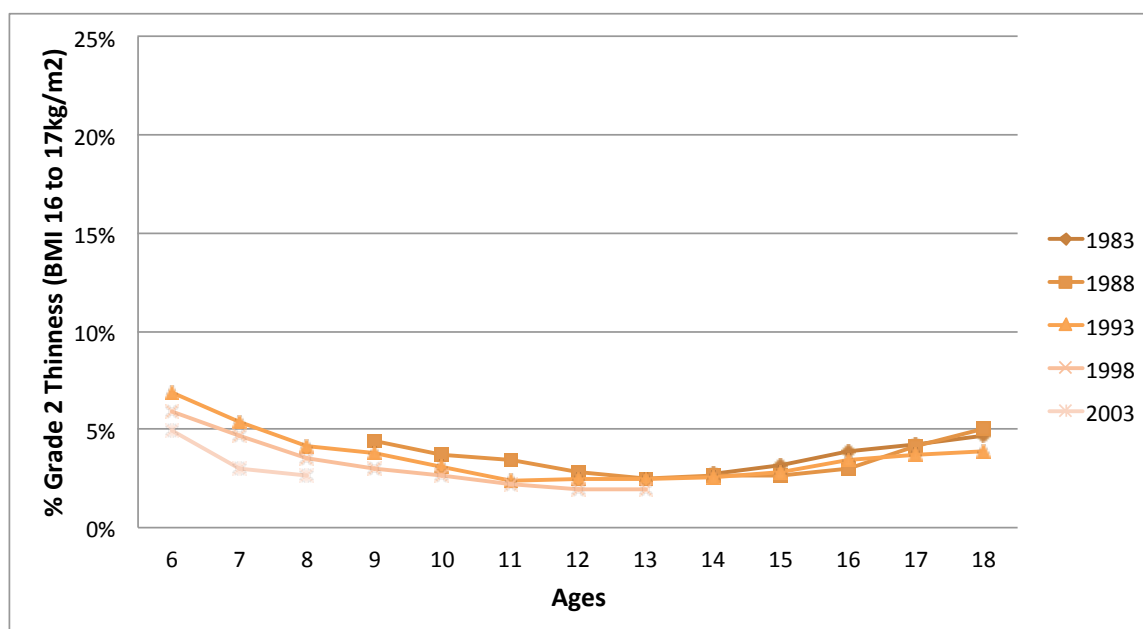
**Figure 15** Age-cohort obese (BMI > 30kg/m<sup>2</sup>) trends among children aged 6 to 18 born from 1983 to 2003 in Singapore



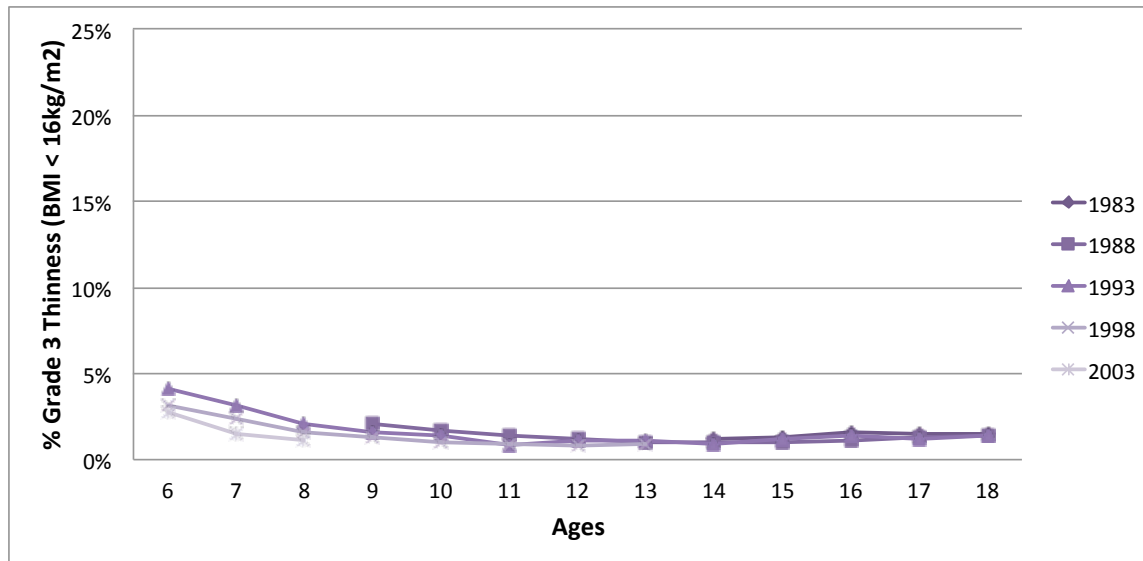
**Figure 16** Age-cohort overweight (BMI 25 to 30kg/m<sup>2</sup>) trends among children aged 6 to 18 born from 1983 to 2003 in Singapore



**Figure 17** Age-cohort grade 1 Thinness (BMI 17 to 18.5kg/m<sup>2</sup>) trends among children aged 6 to 18 born from 1983 to 2003 in Singapore



**Figure 18** Age-cohort grade 2 Thinness (BMI 16 to 17kg/m<sup>2</sup>) trends among children aged 6 to 18 born from 1983 to 2003 in Singapore



**Figure 19 Age-cohort grade 3 Thinness (BMI < 16kg/m<sup>2</sup>) trends among children aged 6 to 18 born from 1983 to 2003 in Singapore**

#### **5.4.2.2 Median polish approach**

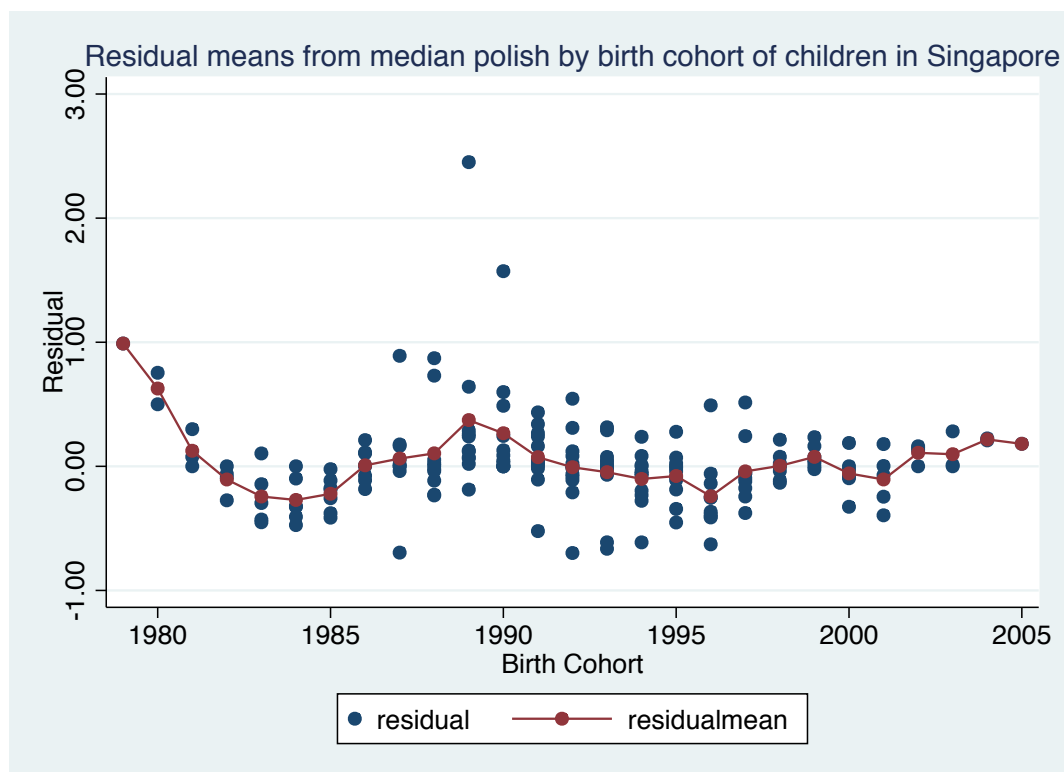
Table 39 is the Age-period contingency table for annual mean % obesity among school-age children in Singapore from 1997 to 2011. Residuals identified (indicative of magnitude of cohort effects) from the median polish analysis showed a marked deviation from zero indicating the presence of cohort effects on obesity rates of students born in 1980 to 2003 (Table 40 and Figure 20). Findings suggested that children born from 1980 to 1986 had a stronger protective effect in reducing obesity rates. This influence varied over the years.

**Table 39 Age-period contingency table for mean % obesity among children aged 6 to 18 in Singapore from 1997 to 2011**

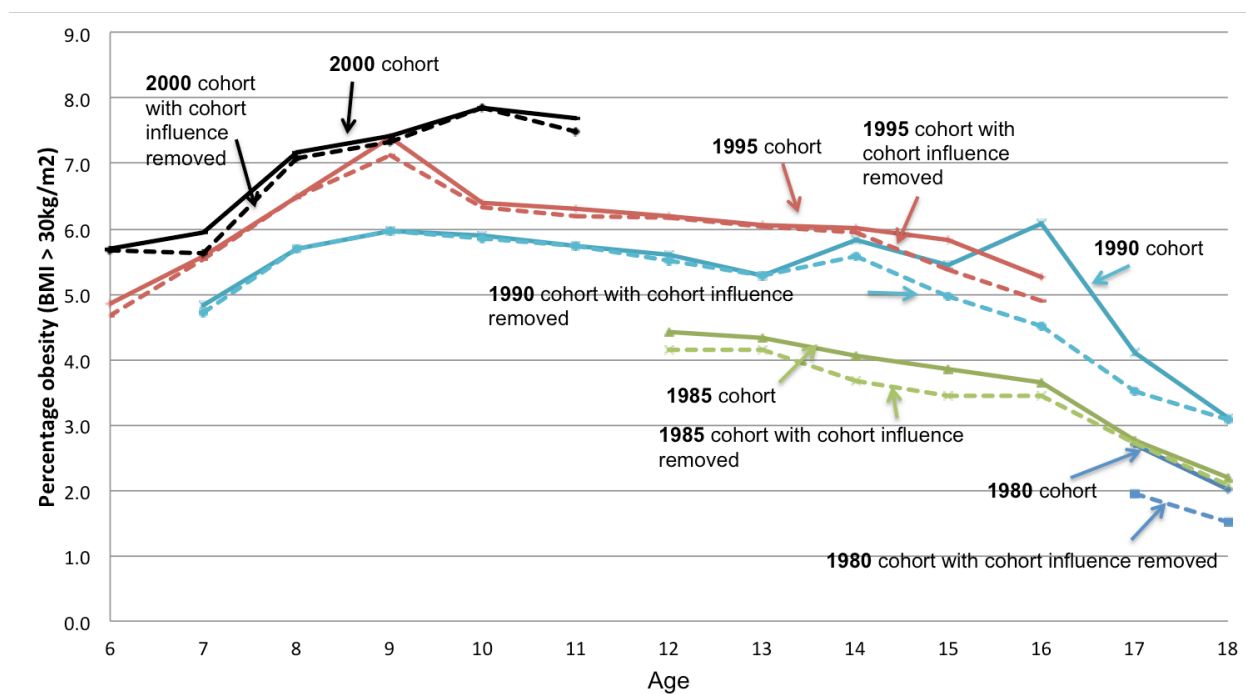
Age	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
6	4.60%	4.65%	4.75%	4.55%	4.85%	4.81%	5.30%	5.79%	5.70%	5.70%	5.51%	6.26%	6.28%	7.06%	6.98%
7	4.83%	5.18%	5.01%	5.14%	5.37%	5.57%	5.67%	6.79%	5.80%	6.10%	5.95%	6.44%	6.64%	7.49%	7.38%
8	5.53%	5.70%	5.90%	5.95%	6.14%	6.31%	6.49%	7.53%	6.50%	6.72%	7.07%	7.17%	7.16%	8.13%	7.93%
9	5.53%	6.03%	5.97%	6.10%	6.19%	6.39%	6.66%	7.41%	6.30%	6.77%	7.13%	7.52%	7.41%	8.23%	8.17%
10	5.35%	5.55%	5.79%	5.90%	6.08%	5.98%	6.42%	6.87%	6.40%	6.33%	6.87%	7.37%	7.34%	7.85%	7.82%
11	4.95%	5.23%	5.45%	5.64%	5.73%	5.85%	6.08%	6.60%	6.10%	6.31%	6.35%	7.07%	6.99%	7.60%	7.68%
12	4.41%	5.01%	5.25%	5.19%	5.66%	5.60%	5.86%	6.16%	5.80%	5.98%	6.20%	6.22%	6.48%	7.24%	7.11%
13	3.95%	4.33%	4.69%	4.94%	5.02%	5.23%	5.29%	5.85%	5.40%	5.69%	5.64%	6.06%	6.07%	6.39%	6.74%
14	3.59%	3.78%	4.05%	4.51%	4.73%	4.74%	4.85%	5.83%	5.20%	5.53%	5.66%	5.82%	6.02%	5.89%	6.24%
15	3.51%	3.57%	3.79%	3.86%	4.60%	4.62%	4.58%	5.43%	5.40%	5.51%	5.66%	5.90%	5.96%	5.83%	5.84%
16	3.13%	3.27%	3.25%	3.53%	3.64%	4.18%	4.21%	4.47%	4.90%	6.09%	5.13%	5.48%	5.35%	5.39%	5.25%
17	2.69%	2.47%	2.29%	2.54%	2.64%	2.75%	2.85%	2.82%	3.80%	5.78%	4.11%	3.63%	3.87%	3.82%	3.79%
18	2.27%	2.01%	1.77%	1.78%	1.84%	1.79%	2.19%	2.67%	3.30%	3.54%	3.11%	3.11%	2.69%	3.08%	3.08%

**Table 40 Birth cohort effect on obesity rates of children aged 6 to 18 in Singapore**

<b>Birth cohort</b>	<b>Cohort Effect</b>	<b>Std. Err.</b>	<b>t</b>	<b>P&gt;t</b>	<b>[95% Confidence Interval]</b>	
<b>1980</b>	-0.36	0.38	-0.95	0.34	-1.12	0.39
<b>1981</b>	-0.86	0.36	-2.4	0.02	-1.57	-0.15
<b>1982</b>	-1.10	0.35	-3.15	<0.01	-1.78	-0.41
<b>1983</b>	-1.23	0.34	-3.61	<0.01	-1.91	-0.56
<b>1984</b>	-1.26	0.34	-3.75	<0.01	-1.92	-0.60
<b>1985</b>	-1.21	0.33	-3.64	<0.01	-1.87	-0.55
<b>1986</b>	-0.98	0.33	-2.97	<0.01	-1.63	-0.33
<b>1987</b>	-0.93	0.33	-2.82	<0.01	-1.57	-0.28
<b>1988</b>	-0.88	0.33	-2.71	0.01	-1.53	-0.24
<b>1989</b>	-0.62	0.33	-1.9	0.06	-1.26	0.03
<b>1990</b>	-0.72	0.32	-2.23	0.03	-1.36	-0.08
<b>1991</b>	-0.92	0.32	-2.83	0.01	-1.55	-0.28
<b>1992</b>	-1.00	0.32	-3.08	<0.01	-1.63	-0.36
<b>1993</b>	-1.04	0.32	-3.21	<0.01	-1.67	-0.40
<b>1994</b>	-1.09	0.32	-3.37	<0.01	-1.73	-0.45
<b>1995</b>	-1.07	0.33	-3.28	<0.01	-1.71	-0.43
<b>1996</b>	-1.23	0.33	-3.77	<0.01	-1.88	-0.59
<b>1997</b>	-1.03	0.33	-3.14	<0.01	-1.68	-0.38
<b>1998</b>	-0.99	0.33	-2.98	<0.01	-1.64	-0.33
<b>1999</b>	-0.91	0.33	-2.74	0.01	-1.57	-0.26
<b>2000</b>	-1.05	0.34	-3.11	<0.01	-1.71	-0.38
<b>2001</b>	-1.10	0.34	-3.21	<0.01	-1.77	-0.42
<b>2002</b>	-0.88	0.35	-2.53	0.01	-1.57	-0.19
<b>2003</b>	-0.89	0.36	-2.48	0.01	-1.60	-0.18
<b>2004</b>	-0.77	0.38	-2.03	0.04	-1.53	-0.02
<b>2005</b>	-0.81	0.44	-1.83	0.07	-1.68	0.06



**Figure 20** Residual means from median polish by birth cohort of children aged 6 to 18 in Singapore



**Figure 21** Age-period obesity trends of children born in 1980, 1985, 1990, 1995 and 2000 with and without cohort effects

The residuals were subtracted from obesity rates in the original contingency table to illustrate the age-period obesity trends for children born in 1980, 1985, 1990, 1995, 2000 with and without cohort effects (Figure 21). From these years selected for comparison, results showed that the percentage obese in 1980 birth cohort was lower when cohort influence was removed. Cohort effects in the 1998 and 1990 cohorts were varied by age. Fewer cohort influences were observed for more recent cohort in 1995 and 2000 in general.

#### **5.4.3 Difference in classification of obesity**

The percentage of obese school-age girls and boys classified using international cut offs of BMI greater than  $30 \text{ kg/m}^2$  were significantly lower in all years when compared to students classified by nutritional status ( $>120\%$  of standard), as reported in annual school health reports in the same periods (Table 41 and Table 42). In 2006 to 2008, the percentage of obese boys in Primary 6 (aged 7) was more than 10% higher when determined using nutritional cut offs when classified using international BMI-for-age cut offs.

**Table 41 Percentage of girls in Singapore classified as "obese" using WHO Child Growth Standards as compared if classified using Nutrition Status cut-offs from 1997 to 2010**

GIRLS	Primary 1 (age 7)		Primary 6 (age 12)		Secondary 4 (age 16)	
	WHO BMI cut-off (>30kg/m <sup>2</sup> )	Nutritional status (>120% of standard)	WHO BMI cut-off (>30kg/m <sup>2</sup> )	Nutritional status (>120% of standard)	WHO BMI cut-off (>30kg/m <sup>2</sup> )	Nutritional status (>120% of standard)
1997	3.73%	10.87%	3.43%	11.51%	2.49%	12.18%
1998	4.08%	10.38%	3.75%	12.02%	2.47%	11.60%
1999	3.91%	9.85%	4.03%	11.92%	2.19%	11.36%
2000	3.95%	10.74%	3.87%	12.88%	2.59%	12.73%
2001	4.13%	10.37%	4.02%	12.51%	2.45%	N/A
2002	4.40%	10.38%	4.11%	12.46%	2.87%	N/A
2003	4.56%	10.72%	4.40%	12.68%	3.14%	N/A
2004	5.45%	10.77%	4.68%	12.05%	3.03%	N/A
2005	4.62%	11.21%	4.37%	12.36%	3.65%	N/A
2006	5.04%	12.24%	4.45%	13.22%	5.01%	N/A
2007	4.73%	11.49%	4.36%	13.09%	3.69%	N/A
2008	4.95%	11.11%	4.71%	12.86%	4.05%	N/A
2009	4.90%	10.80%	4.90%	N/A	4.01%	N/A
2010	6.01%	10.59%	5.51%	N/A	3.84%	N/A

**Table 42 Percentage of boys in Singapore classified as "obese" using WHO Child Growth Standards as compared if classified using Nutrition Status cut-offs from 1997 to 2010**

BOYS	Primary 1 (age 7)		Primary 6 (age 12)		Secondary 4 (age 16)	
	WHO BMI cut-off (>30kg/m <sup>2</sup> )	Nutritional status (>120% of standard)	WHO BMI cut-off (>30kg/m <sup>2</sup> )	Nutritional status (>120% of standard)	WHO BMI cut-off (>30kg/m <sup>2</sup> )	Nutritional status (>120% of standard)
1997	5.86%	10.57%	5.32%	14.10%	3.73%	12.23%
1998	6.20%	11.31%	6.16%	15.47%	4.03%	12.03%
1999	6.07%	10.57%	6.37%	14.99%	4.25%	11.84%
2000	6.23%	10.80%	6.42%	16.29%	4.40%	13.43%
2001	6.55%	11.18%	7.20%	17.05%	4.81%	N/A
2002	6.65%	11.18%	6.96%	16.51%	5.41%	N/A
2003	6.71%	11.44%	7.21%	16.24%	5.23%	N/A
2004	8.04%	11.71%	7.55%	15.87%	5.92%	N/A
2005	6.83%	12.31%	7.12%	16.58%	6.06%	N/A
2006	7.08%	13.08%	7.43%	18.32%	7.14%	N/A
2007	7.08%	12.82%	7.92%	18.28%	6.52%	N/A
2008	7.82%	12.83%	7.62%	17.72%	6.89%	N/A
2009	8.27%	12.12%	7.96%	N/A	6.66%	N/A
2010	8.89%	12.18%	8.88%	N/A	6.94%	N/A



## 5.5 Discussion

### 5.5.1 Is there a possible levelling of the obesity situation in Singapore and do trends differ for boys and girls?

This study detected an upward shift in obesity rates for school-age children aged 6 to 12 and a levelling off between ages 13 to 18, occurring at about the same time around the year 2008. The same growth pattern was observed for boys and girls. This suggested that the environment was not influencing the age groups in a similar manner, although given that the change in trend happened at the same time, strong period effects were likely in effect. While this study did not set out to determine the casual factors for the obesity plateau in 2008, it was postulated that national and school health promotion policies had played an important role in shaping the “obesogenic” environment in Singapore although global evidence suggested that, when implemented alone, school diet and physical activity related policies appear insufficient to prevent or treat overweight or obesity in children (224). However, they do appear to have an effect when developed and implemented as part of a more extensive intervention programme (224).

As mentioned in the introduction of this Chapter, there are few longitudinal studies on obesity in Singapore and thus limited information is available to explain factors that might have led to the levelling off in 2008. However, what is known from a cross-sectional school health survey in 2006 is that, only 40% and 46% of the Secondary 1 to Secondary 4 students (ages 13-16 years old) consumed the daily recommended 2 servings of fruit and vegetables daily respectively. 29% of them consumed sweetened drinks more than once a day and 52% of them consumed deep fried food more than twice a week (225). Concerned with these findings, the HPB adopted a multi-pronged approach comprising various strategies to promote health eating

among children and youth in Singapore and began to introduce a series of innovative school-based nutrition initiatives after 2006 (226) with an objective to increase consumption of adequate whole-grains, fruits and vegetables among children.

Briefly, these include programmes such as “The Fruittie Veggie Bites programme”, “The Health Food Race” and joint collaborations with the Ministry of Education to incorporate healthy eating messages in the health education and home economics curricular (226). At the same time, nutrition guidelines on creating health and nutritious menus in the school tuck shops were provided to ensure that the staff and students had access to healthy food choices in school. Under the Model School Tuck Shop Programme (MSTP) since 2003, an approved drinks list was also available to guide schools to provide suitable drinks for sale. Water coolers were also purposefully installed to encourage students to drink more plain water instead of sugared drinks. Schools that complied with these nutritional guidelines would achieve the Model School Tuck Shop Award (227). Therefore, it may be reasonable to suggest that these initiatives have contributed to the levelling off of obesity in school-age children in 2008.

Similar findings on the possible levelling of the obesity epidemic were reported in the US where rapid increases in obesity prevalence seen in the 1980s and 1990s had not continued in this decade and may be levelling off at about the same in Singapore as detected in our study (6, 228). In Australia, there was plateau in obesity and overweight already from mid- to late-1990s (206, 229) with a fairly consistent trend across all age groups.

An issue rarely addressed in the literature is the evidence for a non-linear, stepwise increase in the prevalence of obesity over time. In Denmark, the epidemic developed in several phases. A long period with a stable prevalence was followed by the first increase related to birth cohorts from the early 1940s and lasted about a decade – resulting in almost a 10-fold increase in the prevalence of obesity. The increase was then followed by another period of stability at this higher level. A second increase began with the birth cohorts from the early 1970s and was even steeper than the first one (194).

Methodologically, one weakness in the Zivot-Andrews Unit Root test is its inability to deal with more than one break in a time series and so in this instance, we would not be able to detect any potential non-linear, stepwise changes as in the situation of Denmark. In addition, in our study, the test was run to detect a structural break in both intercept and slope. If only a break in trend is defined, then the levelling of obesity for boys and girls aged 13 to 18 would have been detected earlier in 2007 and for later for girls aged 6 to 12 in 2009.

### **5.5.2 What are the age, period and cohort effects influencing obesity trends among school-age children in Singapore?**

The analysis shows that there were changes over time of age-specific obesity estimates, thus indicating the presence of cohort and/or period effects in Singapore school-age children. It is likely that both period and cohort effects were in effect given the marked changes over time for different age groups over same time periods (Figure 8). Residual means from median polish of annual obesity rates from 1997 to 2011 confirmed the presence and size of cohort effects with a marked negative effect on obesity rates in the mid-1980s (Figure 20 and Table 40). Youth born in the period 2000 to 2010 were observed to have successively higher body weights than earlier-

born cohorts two decades ago (1980 to 1990), based on the trends observed in cohort-stratified age trends of % obesity and overweight rates (Figure 15 and Figure 16). These effects were attenuated when cohort influences were removed (Figure 21).

Unfortunately, there are few anthropometric longitudinal studies (210, 211) on school-age children in Singapore and a small number of cross-sectional studies (230, 231) prior to this study. For example, it would be important to investigate the neighbourhood effect on obesity of the school environment as the break in obesity trends detected in this study correspond to periods in primary (age 6 to 12), secondary schooling years (age 13 to 16) and junior college/polytechnic education (age 17 to 18). More research into the wider social, environmental, economic, health interventions or events in the past three decades may assist in identifying more specific potential explanatory factors driving these observed trends in age, period, and cohort effects in the future.

Other age-period-cohort findings in Asia include those from Japan, India, China and Thailand. A levelling-off of the mean body height and weight among school children has been observed in Japan (232). In India, evidence for stability in the prevalence has been seen for boys, while an increase has been observed for girls (233, 234). A continuous increase in the epidemic has been seen in adolescents from China (235). In Thailand, newer birth cohorts have a greater value of weight, height and BMI than older cohorts. Prevalence of overweight has also increased with age up to early adolescence, with a subsequent downward trend later in life. Males and females have a different pattern of age effect. Anthropometric parameters of females reached plateau earlier than those of males. Prevalence of overweight of females was lower than

of males and decreased when reaching adolescence. There is a wide gap among children of a country undergoing an economic transition like Thailand (236).

Similarly in Vietnam, a longitudinal study with four birth cohorts: 1981, 1982, 1983 and 1984 followed up in their homes from birth to 10-years old provided evidence of an increasing obesity trend among Vietnamese children, especially when the improvement in living conditions over the past two decades (1975-1995) may be as great as that achieved over the entire previous century. It is important, however, to note that the secular trends observed in Vietnam could also have been more likely driven by the fact that Vietnamese children were finally achieving their genetic growth potential in more recent times of social development as compared to sustained periods of poor nutrition before 1975 (237).

In the first large national study in China to compare BMI and height growth in large national cohorts, from birth throughout childhood, adolescence, and across adult life, secular upward trends in general and abdominal obesity among Chinese children and adolescents from 1993 to 2009 has been detected. Similar to our study, it found that the prevalence of general and abdominal obesity increased more rapidly in girls than in boys when the participants were in their childhood of 6–12 years, but the trend reversed itself when subjects were in their adolescence.

### **5.5.3 Is there a difference in estimating the extent of the obesity situation in school-age children in Singapore from 1997 to 2011 using international BMI age- and gender-specific cut offs based on WHO Child Growth Standards versus the existing practice of using nutritional status?**

The extent of obesity among school-age children at primary 1 (aged 7), 6 (aged 12) and secondary 4 (aged 16) from 1997 to 2011 could be deemed more severe when measured using a nutritional cut-off of greater than 120% of standard as compared to using international BMI-for-age cut offs (Table 41 and Table 42). This is perhaps an illustration of the methodological problem of inconsistency between classifications of childhood obesity as a major obstacle in studying global secular trends for younger age groups (238). In Singapore, BMI for sex- and age-specific percentiles had been used for ease of communicating concerns of severe underweight, overweight and severe overweight. However, when required to assess longitudinal growth in children, the use of percentiles is less than ideal due inherent limitations; for example, the same increments at different percentile levels could correspond to different sizes of change in both Z - scores and absolute measures, and it does not allow for quantifying the change in percentile values near the extremes of the reference distribution. It has been suggested that percentiles should not be used to assess change in status over time, while change in BMI Z-scores is a better measure for such research (171).

There are several advantages of using BMI Z-scores over percentiles as the former are calculated based on the distribution of the reference population (both the mean and the standard deviation), thus, they reflect the reference distribution. As standardised measures, Z-scores are comparable across age, sex and measure. In addition, a group of Z-scores can be subject to summary statistics such as mean and standard deviation (SD) and can be studied as a continuous variable thereby allowing quantification of the growth status of children outside of the normal

percentile ranges (171). An important aspect of the WHO Child Growth Standards is the use of the Z-score system for nutritional status classification. Z-scores are preferred because they permit clinical tracking of patients whose anthropometric classification lies beyond the measurable limits of the percentile range, as happens in the case of severely undernourished or obese children (239).

Local researchers in Singapore have long advocated for the use of the national growth standards in Singapore as a better reflection of the unique growth patterns of the diverse ethnic population make up (75) and the fact that the use of NCHS growth charts as growth standards in Asiatic populations may not be appropriate, and local growth charts should be used whenever they are available (211). Hitherto, results from obesity-related research in Singapore using national reference samples have not been easily comparable with other studies utilising international constituted reference populations such as the WHO child growth standards.

Although WHO BMI classifications are meant to be applicable internationally, there has been strong evidence, including in Singapore, of increased cardiovascular risk factors in Asian populations at BMI values below the cut offs, particularly, for overweight and obesity (151, 240-244). This led to the WHO recommendation to lower the BMI cut-offs for Asian adults, for overweight from 25 to 23 kg/m<sup>2</sup> and for obesity from 30 to 27.5 kg/m<sup>2</sup> during a WHO expert consultation on BMI in Asian populations, which met in Singapore in 2002 (245).

In this study, sex-specific BMI-for-age z-scores and weight classifications were standardised for all students, using the Stata command “zanthro” (172), derived from WHO child

growth standards and international cut-offs so that results can be internationally more comparable. It was not possible to generate sex-specific BMI-for-age z-scores and weight classifications based on local cut-offs, as the Singapore growth reference curves were not included in the zanthro Stata package. Future research on obesity in Singapore for both children and adults should consider reporting their results based on using WHO, IOTF and Singapore cut-offs so that interpretations can be more balanced and yet internationally comparable.

## **5.6 Strengths and limitations of this analysis**

Data that are routinely collected are important in monitoring the health of communities and should be used in the planning of community-based interventions (246). The use of data-mining techniques has previously been shown to be able to facilitate analysis of large amounts of health services data collected by school nurses and yields unique and meaningful results (96). This current PhD study represented the largest pooling of anthropometric data on about 500,000 students each year from 1997 to 2011 that were collected through routine school-based health examinations across about 95% of all primary and secondary schools for all educational levels in Singapore. Physical education instructors conducted health examinations in a standardised manner. Data recording were completed at individual school levels and submitted electronically to the Ministry of Education (MOE), who was responsible for consolidation and data storage.

Previous nationally representative studies in Singapore were often cross-sectional surveys and even when data were collected from a large number of individuals it did not necessarily include many individuals at every age or with a limited number of individuals studies (162, 163, 211). The dataset used in this study did not require a sampling methodology to ensure statistical



power as it utilised the MOE's TAF programme with an estimated national coverage of 95% across all primary and secondary schools in Singapore. Essentially, the dataset included almost all boys and girls in the study time period given that the mean years of schooling among resident Singaporeans is between 8 to 10 years corresponding to six years of primary schooling and four years of secondary schooling (177).

The main limitation of this study is the inability to check the validity of the height and weight measurement recorded, though it may be reasonable to assume that the qualified nurses in the school health teams and trained teachers were accurately measuring the students and accurately entering into the school-based health screening programme system. Physical direct measures for assessing height, weight and BMI have also been shown in a systematic review to be less likely to underestimate weight and overestimate height as compared to self-report measures, although the degree of the trend varied for men and women, and between studies (247). Some may also argue that data mining of routine data may be less accurate than those collected prospectively in carefully executed studies, but this must be balanced against the large amount of information that is readily available, previously not accessible for research purposes.

Other limiting factors to consider include different sampling frames as students were measured at different times of the year and may not be comparable across years and across other national datasets. Also, while all children are likely to start primary school at the same age and progress to the academic level each year, it cannot be assumed that students are necessarily representative of the same age in the same educational level. Also, no attempt was made to evaluate the data quality and accuracy with the schools. In hindsight, the use of BMI-for-age

classification of weight status would not have been able to discriminate between short-term and long-term forms of malnutrition or obesity. Ideally, it would be appropriate to use height-for-age and weight-for-height measurements as the indicators of choice for health screening (248).

Unfortunately height information was not available in the dataset.

## 5.7 Conclusion

Although recent trends in Singapore suggested that prevalence of overweight and obesity has been flattening since 2008, it is also possible that the flattening represented a temporary lull and that without continued efforts we might again see a rise in prevalence (206). It is also relevant to consider whether a stable trend could indicate that the incidence rate of new obesity cases continues at the same high level, since no decline in the prevalence is evident.

Alternatively, the duration of the condition has been shortened, e.g. because of better treatment or higher mortality, although neither of these appears to be a particularly likely explanation for the levelling off. In this case, the incidence rate could theoretically still be increasing even though the prevalence is constant (39, 194).

In closing, I have shown that routinely collected data from school-based health screening programmes can be used for epidemiological growth monitoring in the Singapore context (probably at a lower cost compared with other dedicated cross-sectional or longitudinal study design and even increases the returns on investments into routine school health screening programmes). This study was able to provide useful insights into the age, period and cohort effects during early childhood and adolescence from 1997 to 2011 using such data. While these findings suggested that obesity prevalence among Singapore youth aged 13 to 18 had reach a

plateau from 2008 to 2011 it is worrying that a steeper upward trend was observed for both boys and girls aged 6 to 12 after 2008. More work is required to fully explain these secular trends. Finally, simply observing BMI increases with ageing without considering period and cohort effects may lead to an under- or over-estimation of the obesity situation and prevention of weight gain should adopt a population-wide, life-course approach.

## **Chapter 6: Latent growth trajectories of body mass index in Singapore adolescents from 1990 to 2011**

### **Synopsis**

Previous studies on growth among Singapore children traditionally reported the prevalence % of atypical weight classifications, such as underweight, overweight, in different years without much further information on how children in the entire study grew over the years and whether different groups of students grew differently from each other (210, 211, 249). Findings from the previous Chapter provide additional insights by identifying the possible levelling off in obesity trends among Singapore youth aged 13 to 18 and unfortunately, it also found that there is a steeper upward trend observed for both boys and girls aged 6 to 12 after 2008. To the best of my knowledge, there has not yet been a study in Singapore investigating cohort effects on obesity, therefore, observations that youth born in the period 2000 to 2010 were having successively higher body weights than earlier-born cohorts two decades ago (1980 to 1990), suggest that obesity is affecting recently born Singaporean school-age children to a greater extent than those older.

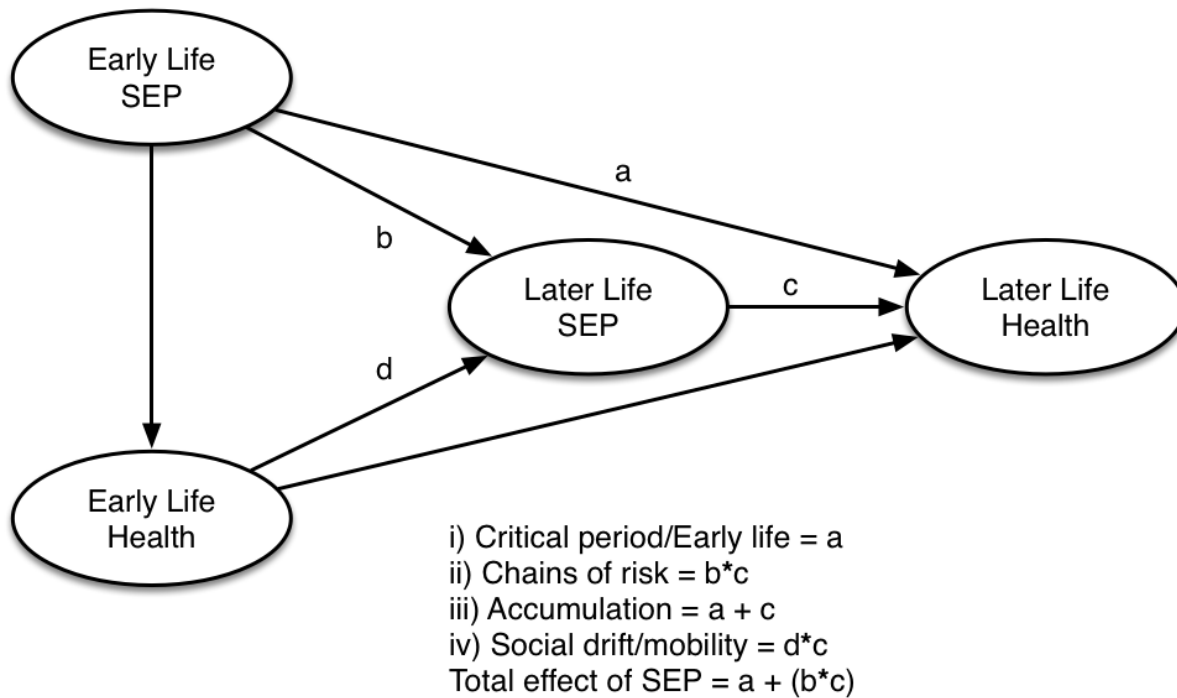
Until now, the only basis for monitoring the impact of national efforts to reduce obesity were the cross-sectional National Health Surveys conducted every 6 years, and these only collect data on adults older than 18 years old. This approach greatly limits knowledge about the aetiology of obesity during childhood and puberty stages until the magnitude of adult obesity is detected through the national health surveys. Therefore, in this Chapter Six, I attempt to characterise latent BMI-for-age z-score trajectories using the routine school-based health screening data from 1990 to 2011.

The reader should note that the next Chapter (Seven) will adopt similar latent growth curve modelling techniques to determine the association of childhood and adolescent BMI Z-score trajectory as a determinant for later life health outcomes (26, 27). That study would also demonstrate how SLLCC could be linked with an existing National Health Survey 2010 respondents' dataset.

## **6.1 Introduction**

The life course approach offers new thinking about how socially patterned exposures during childhood, adolescence, and early adult life can influence adult disease risk and later socioeconomic position, and hence may account for social imbalances in adult health and mortality (53, 166). To date, several theories of association between social economic position (SEP) and health over the life course have been postulated (52), for example, the “early life/critical period”, “chains of risk”, “accumulation of risk” and the “social drift or mobility”, as shown in Figure 22 adapted from (250).

Generally, within epidemiology, creating groups with the same developmental trajectory is increasingly common. It is mostly used as a descriptive tool, but the trajectories are also used either to explore their role as determinants of future health outcomes or as outcome variables to investigate potential predictors of these trajectories (26, 27). For example, when exploring latent trajectories of early-life weight change patterns in the 1946 British Birth Cohort Study, it was found that being overweight throughout early life or becoming overweight in the period from puberty to age 20 years was associated with chronic kidney disease in later life (251).



**Figure 22 Directed acyclic graph of the association between life course social economic position and later life health, adapted from (250)**

The effect of exposures to varying early life social-economic exposures on later life outcomes have been of considerable interest to most life course researchers. Such studies have presented evidence that annual family income during the prenatal period and into the first year of life are associated with adult BMI, whereas income in later periods of childhood is not (252). Other studies show that children who spend a greater proportion of early childhood living in poverty experience accelerated growth trajectories in adolescence based on age- and sex-adjusted BMI percentiles (253). The implication is that promoting upward socioeconomic mobility among disadvantaged families may have a positive impact on obesity-related outcomes in adolescence (254).

However, until now, systematic reviews of evidence supporting models of life-course social economic factors and later life outcomes have not been conclusive because the different methodologies used makes direct comparisons of the conceptual models difficult (255). A 2005 review investigating the existence of life course SES effects on risk of adult cardiovascular diseases suggested that the evidence thus far only modestly supports the existence of life course SES effects on risk of adult CVD, depending on the type of life-course model hypothesised (255). A more recent 2012 systematic review also reported an overall relationship as suggested by the evidence, but results for each life course model were mixed. Social mobility models were generally not supported, but some studies investigating intra-generational mobility did identify an effect. Fewer studies addressed accumulation and pathway effects and the heterogeneity of these studies limited the options for synthesis. The only consistent support in both reviews was for an accumulation effect of socio-economic adversity on cardiovascular disease risk, and moderate support for a latent effect of low childhood SEP on increased cardiovascular disease risk factors, morbidity and mortality (89).

More recent analytical techniques have been developed to allow researchers to conceptualise models that better describe and compare growth and change curves over time within a life span. Some of these life course research methods provide new possibilities to allow the modelling of latent, pathway and cumulative effects in a conceptually coherent manner (23). In the context of obesity research, the relevance of changes during a “critical period” is of importance in relation to their long-term protective or adverse effects on development and subsequent disease risk many years later (87). Socioeconomic factors at different life stages may operate either via social chains of risk or by influencing exposures to causal factors at earlier life

stages that form part of long term biological or psychological chains of risk. Many of the suggested behavioural and social risk factors are highly correlated, or may operate as proximal and distal etiological factors on the same causal pathways (40, 165).

Previous research on the impact of early life developmental trajectories of overweight on later health outcomes has predominately focused on gestation weight, rapid weight gain in early infancy or “catch-up growth” in the first two years of life, timing and peak of adiposity rebound around age 6 when BMI begins to increase following a nadir. Fewer studies concentrate on adolescence as a critical period for obesity, due to it being more temporally proximal to adulthood and thus less suitable for the application of interventions (90), even though these are distinct life stages of childhood from age 6 to 12, and adolescence from 12 to 18, where the individual is undergoing significant psychological and physical changes (91).

Given that the mean length of schooling among resident Singaporeans is between 8 to 10 years, corresponding to six years of primary schooling and four years of secondary schooling (177), it is important to consider childhood and adolescent years as potential critical periods in influencing the development trajectories of growth. In particular, the school environment is critical in promoting physical activity and health food choices, even though more research is required to examine effect of individual and contextual mediating factors on the association or causality of the built environment influence on obesity in school children (256). Central to understanding the impact of environments on obesity is the concept of “obesogenicity”, defined as “the sum of influences that the surroundings, opportunities, or conditions of life have on promoting obesity in individuals or populations” (257). Therefore, it is not surprising that



differential exposures to “obesogenic” (obesity-promoting) elements of school’s physical and unhealthy social environment for a sustained period of time may lead to adopting differential behaviours and increasing risks of undesirable health outcomes in later life. Demands and expectations for academic excellence in secondary or pre-college education may also shape behaviour change and life habits in relation to physical activity, diet, smoking and alcohol.

Obesity and childhood obesity in particular are the focus of many public health promotion efforts in Singapore (80). In 1997, 11.6% of the children and adolescent aged 6 to 18 on average were classified as overweight (equivalent to BMI 25 to  $<30\text{kg/m}^2$  at 18 years old) using international sex-specific BMI-for-age cut-offs. 4.2% were considered obese (equivalent to BMI  $\geq 30\text{kg/m}^2$  at 18 years old). 14 years later, the prevalence of overweight and obesity were increased to 15.9% and 6.7% respectively in 2011. Earlier findings from this thesis suggested that while obesity prevalence among Singapore youth aged 13 to 18 had reached a plateau from 2008 to 2011; it remains worrying that a steeper upward trend was observed for both boys and girls aged 6 to 12 after 2008. More work is required to fully explain these secular trends and a series of questions remains unresolved: Why do some individuals maintain a high or low BMI level throughout childhood and what explains why some individuals change more or less than others, as they grow older? What happens over time? Is growth or BMI change linear?

The purpose of the analysis in this Chapter is therefore to characterise latent BMI-for-age z-score trajectories using routine school-based health screening data from 1990 to 2011 and to determine whether educational transition from primary schools to secondary schools account for shifts in trajectories, and if these patterns differ for boys and girls.

## **6.2 Methods**

### **6.2.1 Data sets**

The Singapore Longitudinal and Life Course Cohort (SLLCC) is the largest longitudinal cohort of youth (ages 7 to 18) in Singapore to-date. It consists of an extensive individual-level dataset of repeatedly measured anthropometric data, from about 2.7 million students born between 1973 to 2003, collected through routine annual school-based health screening in Singapore from 1990 to 2011. The SLLCC provides valuable information regarding anthropometric developments of children and adolescents in Singapore and its effects across the life course (See Chapter Four).

Briefly, the primary sources of the SLLCC dataset were the School Health Service (SHS) database from Health Promotion Board (HPB) and the Trim and Fit (TAF) database from the Ministry of Education (MOE). Both datasets captured information routinely collected from an on-going annual health screening dataset of school children in all primary schools (for ages 6 to 12) and 95% of all secondary schools (for ages 13 to 16) in Singapore. Based on procedures described in Chapter Three, a unique random record identifier was allocated to each student NRIC number (Singapore National Identity Card) so that every record of the same student, regardless of whether his or her data was captured during HPB health screening programme or MOE TAF programme at his or her school, would be linked at the individual level across the different ages that his or her weight/height was recorded during the entire schooling period from age 7 to 16.

A total of 1,013,325 subjects, who had at least five time point measurements of weight and height were included for the analysis in this Chapter. The race and gender make up of this sample compared well with the full SLLCC cohort (Table 43).

**Table 43 Gender and race profile of study sample of students with at least 5 BMI measurements as compared to total SLLCC cohort**

Race group	Study sample (at least 5 BMI measurements)		SLLCC (total cohort)	
	Male (%)	Female (%)	Male (%)	Female (%)
Chinese	380,588 (72.1)	349,069 (71.9)	672,194 (72.1)	626,442 (72.2)
Malay	71,260 (13.5)	65,211 (13.4)	125,389 (13.5)	115,650 (13.3)
Eurasian	1,968 (0.4)	1,896 (0.4)	3,274 (0.4)	3,198 (0.4)
Indonesian	23,956 (4.5)	21,542 (4.4)	34,978 (3.8)	31,845 (3.7)
Indian	42,512 (8.0)	40,452 (8.3)	75,211 (8.1)	71,145 (8.2)
Others	7,849 (1.5)	7,022 (1.4)	20,890 (2.2)	19,550 (2.3)
<b>Total</b>	<b>528,133 (52.1)</b>	<b>485,192 (47.9)</b>	<b>931,936 (51.8)</b>	<b>867,830 (48.2)</b>

Notes:

SLLCC consists of an extensive individual-level dataset of repeatedly measured anthropometric data, from about 2.7 million students born between 1973 to 2003, collected through routine annual school-based health screening in Singapore from 1990 to 2011.

## 6.2.2 Variables

### Anthropometric measures

In SHS examinations, basic measurements (height & weight) were taken to calculate the student's height percentile, weight percentile, BMI, BMI percentile and growth velocity within the year cohort. Vision and audiometry tests were also conducted as well as mandatory vaccinations. A primary physician conducted basic screening to check on heart, lung capacity as well as assessing the growth of the student, for example, puberty staging. A trained nurse determined weight and height. In TAF examinations, physical education teachers took basic anthropometric measurements (height & weight) using calibrated weighing and height measurement machines. Students who were found to be underweight or overweight or obese

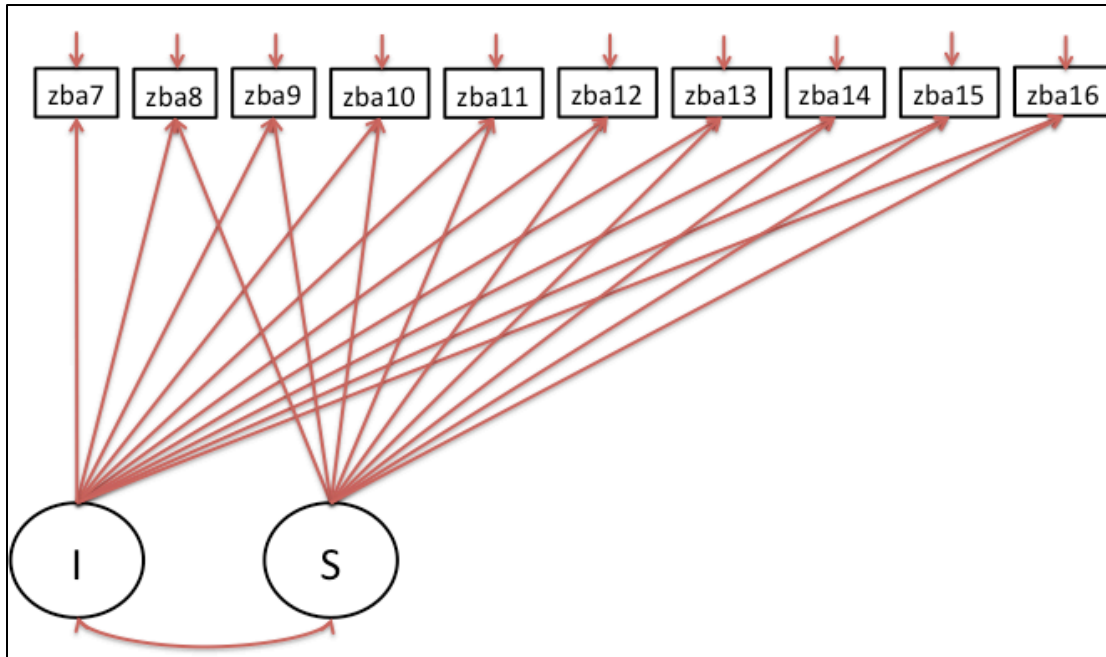
were referred to the Nutrition Center at the Health Promotion Board School Health Service centre for follow-up (See previous Chapter Three).

### **6.2.3 Data preparation**

Sex-specific BMI-for-age z-scores were standardised for all students using the Stata command “zanthro” (172). This extension converts child anthropometric data to Z-scores using the LMS method and the reference data available from the 2000 CDC Growth Reference, the British 1990 Growth Reference, the WHO Child Growth Standards, the WHO Reference 2007, the UK-WHO Preterm Growth Reference, and the UK-WHO Term Growth Reference. For this study, standardised BMI-for-age Z-scores were derived from WHO child growth standards so that results can be internationally more comparable.

### **6.2.4 Statistical analysis methods**

Standard latent class analysis (LCA) models were initially used to study growth patterns of school-age children from age 7 to 16. Detailed specifications of the LCA had been described previously (85, 148). In this study, a simple two-factor linear model was first fitted to determine variability in initial average mean level of BMI-for-age Z-scores (intercept) at age 7 and rate of change in anthropometric measures (slope) over 10 annually measured time points until age 16 (Figure 23). Given that weight and height was measured annually (assumed to be approximately equally spaced occasions as a unit of time metric), all models adopted a fixed factor loading corresponding to the number of years since age 7. Only SLLCC subjects with at least five time point measurements were included in our study population, the analysis also tested for non-linear trajectories in order to provide additional information about the shape of growth over time.

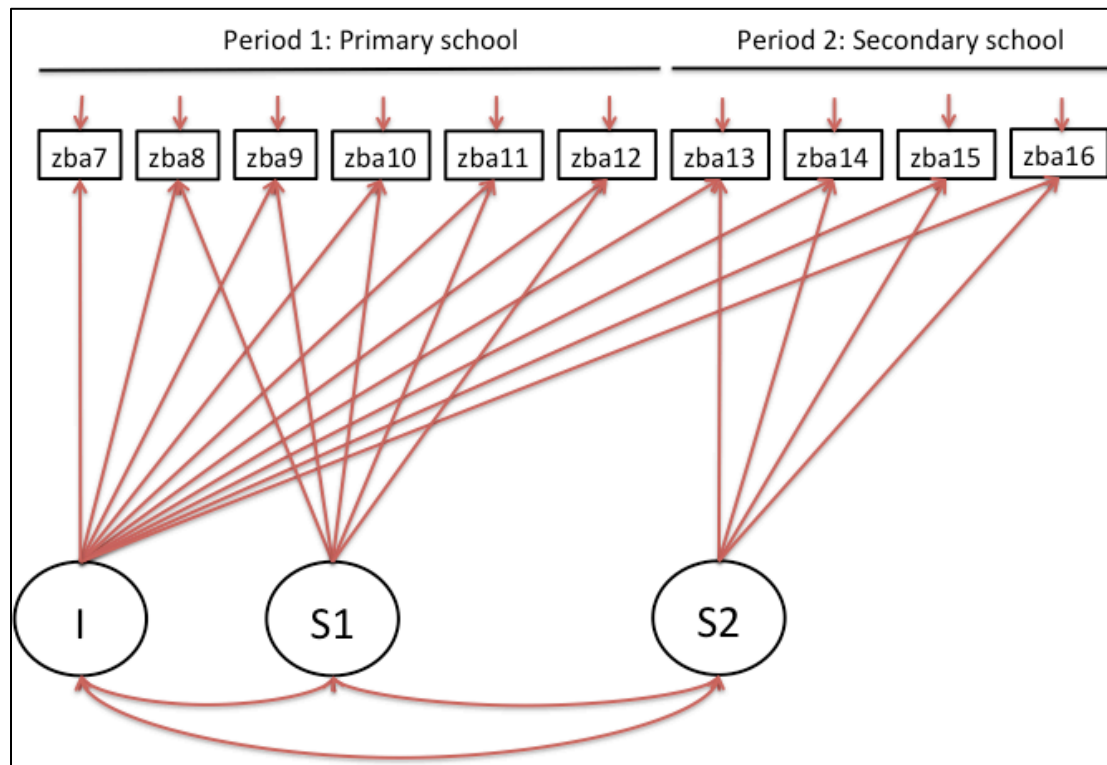


**Figure 23** Example of linear latent class growth model with continuous BMI-for-age Z-score, SLLCC, 1990 to 2011

In order to estimate whether educational transition from primary schools to secondary schools account for shifts in trajectories, piecewise growth models (Figure 24) and growth models for two parallel processes for continuous BMI Z-scores were fitted (Figure 25).

In the piecewise growth model, different phases of development were captured by more than one slope growth factor. The first model specified a linear growth model for the first phase of development, which includes the first six time points (age 7 to 12 as per primary schooling period). The second specified a linear growth model for the second phase of development, which includes the last four time points (age 13 to 16 as per secondary schooling period). Quadratic terms and the gender covariate were added sequentially to improve model fit. The timings of the two phases were determined *a priori*. In all scenarios, we assumed that there was only one starting intercept at age 7, which might influence the rate and shape of change during primary

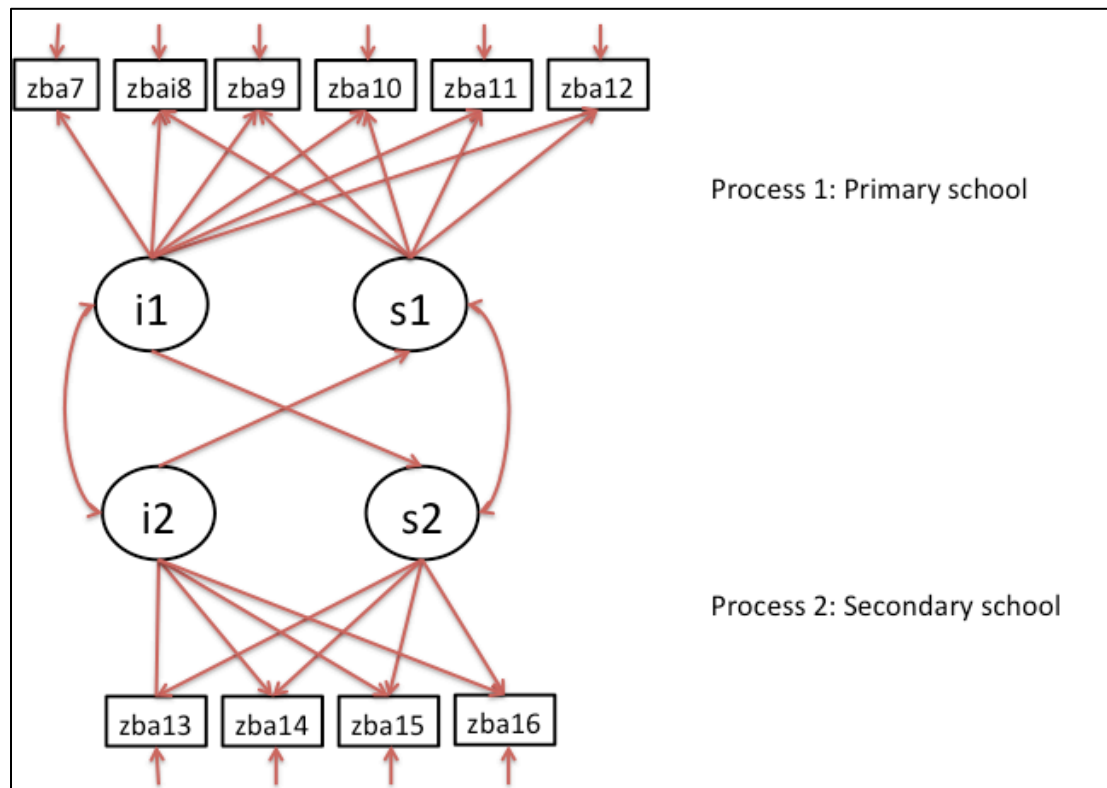
school and secondary school. It was also postulated that the rate and shape of change in the second phase might be influenced by the rate and shape of change in the first phase.



**Figure 24** Example of piecewise linear latent class growth model with continuous BMI-for-age Z-score, SLLCC, 1990-2011

In the growth model for two parallel processes (Figure 25), the terms  $i_1$  and  $s_1$  referred to the intercept and slope growth factors for the first linear growth model. The terms  $i_2$  and  $s_2$  referred to the intercept and slope growth factors for the second linear growth model. For both growth models, the time scores of the slope growth factors were fixed at 0, 1, 2, 3, 4 and 5 to define a linear or quadratic growth model with equidistant time points. In addition, regressions of the slope growth factor for each process on the intercept growth factor of the other process were included. In this scenario, we assumed different starting intercepts at age 7 and age 13, which

may influence only the rate of change of both primary and secondary schooling phases in parallel.



**Figure 25** Example of linear latent class growth model with two parallel processes for continuous BMI-for-age Z-score with regression among random effects, SLLCC, 1990-2011

Tests of model fit were compared utilising standard goodness-of-fit indices such as Bayesian Information Criteria (BIC), Root Mean Square Error Of Approximation (RMSEA), CFI/TLI and Standardised Root Mean Square Residual (SRMSR). As a guiding rule of thumb, a good model fit was deemed to be obtained when CFI/TLI values were over 0.96; RMSEA should be below 0.6; the SRMSR was less than 0.5 and a lower BIC value as compared to other models.

Lastly, latent class growth mixture models (LCGMM) were employed to characterise latent BMI-for-age Z-score trajectories using routine school-based health screening data from 1990 to 2011 (258). LCGMM is a semi-parametric statistical technique used to analyse longitudinal data. It is used when the data follow a pattern of change in which both the strength and the direction of the relationship between the independent and dependent variables differ across cases (258). The analysis was aimed to identify distinct subgroups of individuals following a distinct pattern of change over age or time on a variable of interest.

LCGMMs were fitted to characterise the optimal number of latent trajectories of BMI-for-age z-scores over time from ages 7 to 16. Models with two to six classes were estimated, beginning with the simplest model. Model fit for each of the 5 models was evaluated, in part, using the Bayesian Information Criterion (BIC) (259). Successive comparisons of the BIC were made beginning with the 2-class model, with lower values suggesting better model fit. The final selection of the optimal number of latent classes would be dependent on the point in which the BIC values start to level off. Finally, the models were visually inspected for their theoretical and practical coherence with a preference for simpler and more parsimonious models (259). Patterns of growth trajectories were found to differ between males and females, so separate longitudinal latent class analyses were conducted. Posterior probabilities were derived to quantify the probability with which an individual with a given early-life overweight pattern belonged to each latent class.

For all models, data missingness was handled using full information maximum likelihood under the assumption of missing at random. Mplus software version 6.12 was utilised to conduct



these analyses. Mplus is a latent variable modelling program with a wide variety of analysis capabilities (148) and was used as the main statistical software, together with Stata (149).

## 6.3 Results

### 6.3.1 General analysis

Of the original 2,711,088 students in SLLCC, 911,322 (33.6% of total) had only one BMI measurement between ages 6 to 18 (during their primary and secondary schooling period). For the purposes of this study analysis, 1,013,316 (37.4% of total) students with at least five out of 12 maximum BMI measurement (or BMI Z-score) were included in the latent growth modelling so as to fulfil the minimum covariance coverage value of 0.100. The gender and race distribution of the study sample is described in Table 43. There were no significant differences in means between study sample population and original SLLCC population for both men ( $p=0.20$ ) and women ( $p=0.20$ ).

Table 44 and Table 45 describe summary statistics of BMI-for-age Z-scores and its distribution by age, gender and race groups. Table 46 shows median BMI-for-age Z-score by gender and race groups. An average kurtosis value of 2.69 suggested slightly light-tailed distribution of Z-scores at all ages with a symmetric spread (mean skewness = 0.02).

In general, girls had a lower BMI Z-score than boys at all ages with lower values at younger (7 to 8 years) increasing until 11 to 12 years old before declining at older ages (15 to 16 years) (Figure 26). When growth patterns are disaggregated by race groups, differential rates were observed. For all race groups, median Z-scores were increasing at similar rates from age 7

to 10 but from ages 11 onwards, Chinese youth recorded a lower dip from age 12 to 16 as compared to other races (Figure 27).

**Table 44 Summary statistics of study sample of SLLCC that has at least 5 BMI measurements from age 7 to 16**

<b>BMI Z-score at age</b>	<b>No. Of observation</b>	<b>Median</b>	<b>Mean</b>	<b>Std. Dev.</b>	<b>1st Quartile</b>	<b>3rd Quartile</b>	<b>Skewness<sup>a</sup></b>	<b>Kurtosis<sup>b</sup></b>	<b>% Missing</b>
<b>7</b>	647,205	-0.30	-0.16	1.45	-1.14	0.74	0.37	3.15	36.13
<b>8</b>	641,674	-0.12	0.02	1.54	-1.08	1.10	0.21	2.69	36.68
<b>9</b>	680,000	0.04	0.13	1.57	-1.04	1.32	0.03	2.46	32.89
<b>10</b>	713,265	0.23	0.22	1.59	-0.98	1.50	-0.13	2.37	29.61
<b>11</b>	752,019	0.22	0.19	1.58	-0.99	1.46	-0.18	2.38	25.79
<b>12</b>	782,848	0.28	0.22	1.53	-0.86	1.41	-0.26	2.54	22.74
<b>13</b>	712,605	0.07	0.08	1.47	-0.96	1.19	-0.13	2.62	29.68
<b>14</b>	683,198	-0.10	-0.05	1.40	-1.01	0.94	0.00	2.75	32.58
<b>15</b>	647,750	-0.22	-0.14	1.35	-1.06	0.75	0.13	2.90	36.08
<b>16</b>	551,985	-0.30	-0.21	1.33	-1.12	0.64	0.22	2.99	45.53
<b>Total n</b>	1,013,325								

Notes:

SLLCC consists of an extensive individual-level dataset of repeatedly measured anthropometric data, from about 2.7 million students born between 1973 to 2003, collected through routine annual school-based health screening in Singapore from 1990 to 2011.

<sup>a</sup> –Skewness measures the degree and direction of asymmetry. A symmetric distribution such as a normal distribution has a skewness of 0

<sup>b</sup> – Kurtosis is a measure of the heaviness of the tails of a distribution. A normal distribution has a kurtosis of 3

**Table 45 Mean BMI-for-age Z-score distribution by age, gender and race groups in the study sample of SLLCC that has at least 5 BMI measurements from age 7 to 16**

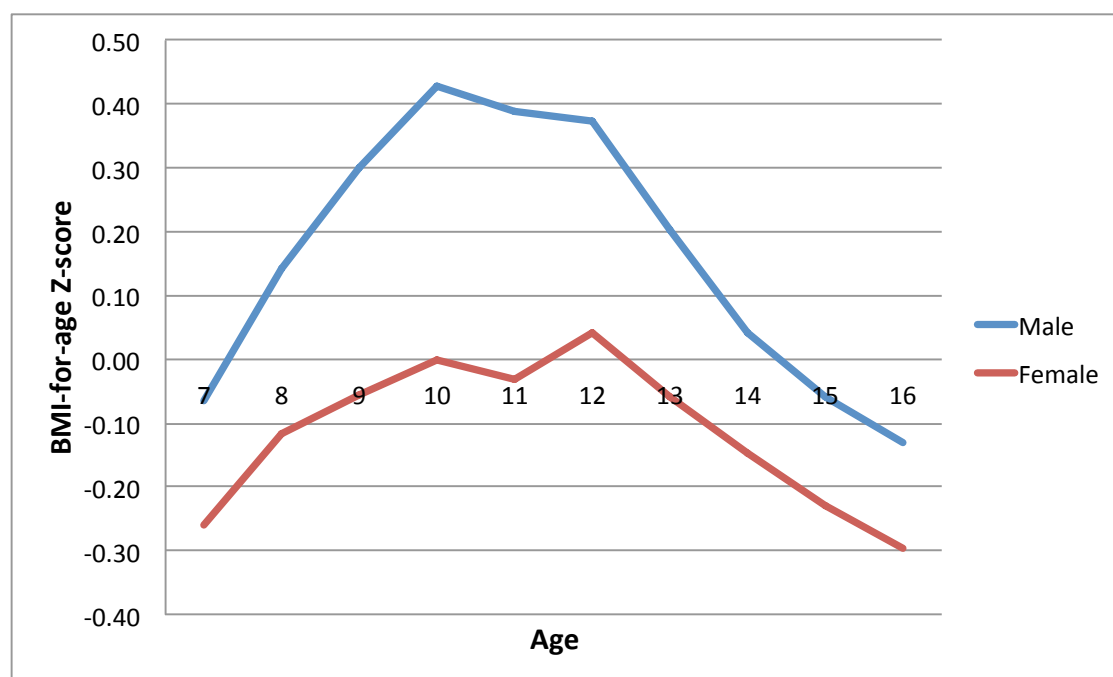
<b>Mean BMI Z-score at age</b>	<b>Male</b>	<b>Female</b>	<b>Chinese</b>	<b>Malay</b>	<b>Eurasian</b>	<b>Indonesian</b>	<b>Indian</b>	<b>Others</b>
<b>7</b>	-0.06	-0.26	-0.16	-0.16	-0.11	-0.10	-0.19	0.14
<b>8</b>	0.14	-0.12	0.01	0.01	0.05	0.04	0.02	0.35
<b>9</b>	0.30	-0.05	0.12	0.14	0.15	0.13	0.15	0.49
<b>10</b>	0.43	0.00	0.21	0.23	0.23	0.18	0.24	0.57
<b>11</b>	0.39	-0.03	0.17	0.22	0.17	0.17	0.23	0.53
<b>12</b>	0.37	0.04	0.20	0.23	0.27	0.21	0.27	0.52
<b>13</b>	0.20	-0.06	0.04	0.17	0.14	0.15	0.18	0.38
<b>14</b>	0.04	-0.15	-0.10	0.08	0.03	0.07	0.06	0.25
<b>15</b>	-0.06	-0.23	-0.19	0.01	0.00	0.01	-0.03	0.13
<b>16</b>	-0.13	-0.30	-0.27	-0.04	-0.05	-0.04	-0.10	0.05

**Table 46 Median BMI-for-age Z-score distribution by age, gender and race groups in the study sample of SLLCC that has at least 5 BMI measurements from age 7 to 16**

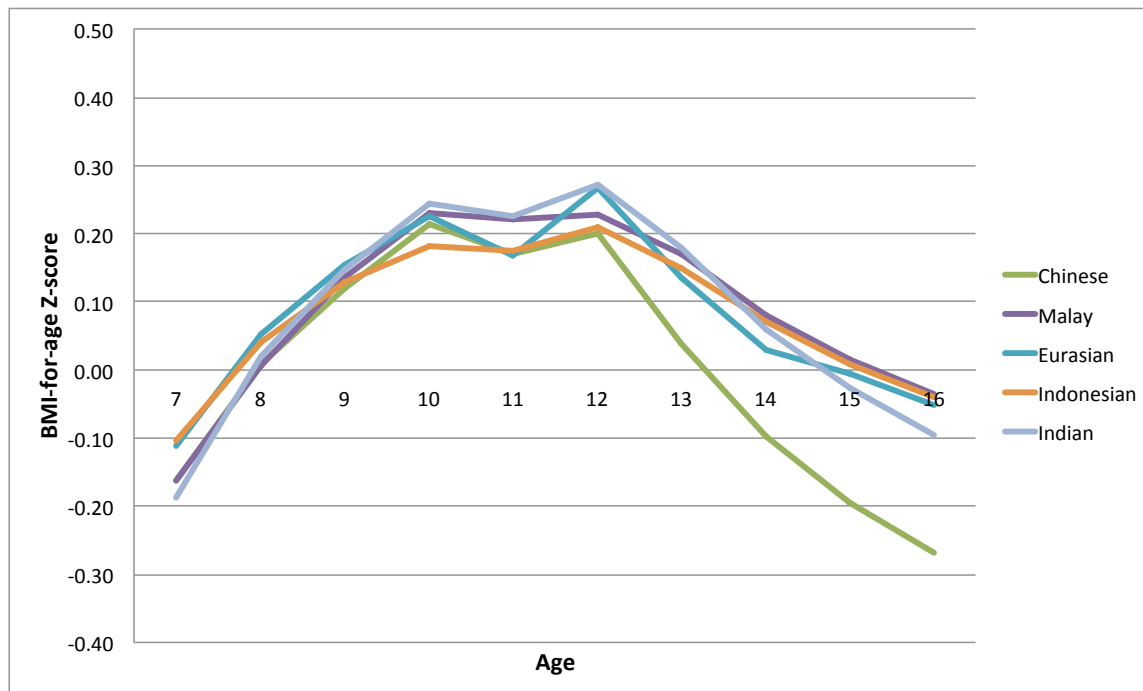
Median BMI Z-score at age	Male	Female	Chinese	Malay	Eurasian	Indonesian	Indian	Others
7	-0.25	-0.36	-0.29	-0.37	-0.27	-0.34	-0.34	-0.01
8	-0.02	-0.21	-0.11	-0.24	-0.13	-0.20	-0.05	0.29
9	0.24	-0.13	0.04	-0.06	0.03	-0.07	0.19	0.51
10	0.50	-0.01	0.23	0.13	0.22	0.04	0.39	0.67
11	0.52	-0.04	0.21	0.17	0.15	0.07	0.40	0.64
12	0.52	0.08	0.27	0.22	0.33	0.15	0.47	0.63
13	0.23	-0.06	0.03	0.12	0.14	0.09	0.30	0.41
14	0.01	-0.19	-0.15	-0.01	-0.02	-0.02	0.11	0.24
15	-0.12	-0.29	-0.26	-0.11	-0.07	-0.10	-0.03	0.11
16	-0.19	-0.38	-0.35	-0.17	-0.12	-0.16	-0.12	0.00

Notes:

SLLCC consists of an extensive individual-level dataset of repeatedly measured anthropometric data, from about 2.7 million students born between 1973 to 2003, collected through routine annual school-based health screening in Singapore from 1990 to 2011.



**Figure 26 Mean BMI-for-age Z-score by gender in the study sample of SLLCC that has at least 5 BMI measurements from age 7 to 16**



**Figure 27 BMI-for-age Z-score distribution by race groups in the study sample of SLLCC that has at least 5 BMI measurements from age 7 to 16**

### 6.3.2 Latent class analysis

Eight growth models (combinations of linear, quadratic, piecewise, two parallel processes, finite mixtures, with and without covariates) were fitted to estimate the development of students BMI Z-score change over time. Results of goodness-of-fit indices for each model are presented in Table 47. More detailed findings on LCGMM are presented in the next section.

Results from indicators of model fit (Table 47) suggested that the underlying anthropometric changes in Singapore school-age children from ages 7 to 16 can be best explained by a piecewise quadratic growth model (Table 48) without consideration of the finite growth mixture approach yet. This best fit model estimated that the mean BMI Z-score at age 7 among the cohort was -0.022, within normal weight range of (BMI: 18.5 to <25 kg/m<sup>2</sup> at 18

years). The rate of change (slope factor) in the first six years of primary schooling was increasing at 0.137 standard deviation of BMI Z-score annually with a slight plateau at about age 12 to 13. Subsequently, there is a statistically significant decline of -0.119 standard deviation of BMI Z-score unit until age 16. Being female had a protective effect of lowering mean BMI at age 7 ( $p < 0.05$ ). Interaction between slope and quadratic terms were small but significant (Table 48). The variance on the intercept term was 1.903, suggesting that more explanatory covariates may be required beyond gender effects.

**Table 47 Goodness of fit indices of 7 latent class growth models using study sample of SLLCC that has at least 5 BMI measurements from age 7 to 16**

Model type	BIC <sup>a</sup>	RMSEA <sup>b</sup>	CFI <sup>c</sup>	TLI <sup>d</sup>	SRMR <sup>e</sup>
<b>Linear</b>	14864343	0.116	0.935	0.942	0.070
<b>Quadratic</b>	14379424	0.065	0.981	0.982	0.022
<b>Quadratic with covariate</b>	14362008	0.061	0.981	0.980	0.020
<b>Piecewise linear</b>	14385948	0.066	0.981	0.981	0.030
<b>Piecewise quadratic<sup>f</sup></b>	14201313	0.023	0.998	0.998	0.005
<b>Linear with 2 processes</b>	14576975	0.095	0.962	0.961	0.032
<b>Quadratic with 2 processes</b>	14231911	0.038	0.995	0.994	0.007

Notes:

<sup>a</sup> BIC = Bayesian Information Criterion; lower values suggest better model fit

<sup>b</sup> RMSEA = Root Mean Square Error Of Approximation

<sup>c</sup> CFI = Comparative Fit Index. Range from 0 to 1 with higher values indicating better fit

<sup>d</sup> CFI = Tucker Lewis Index. Range from 0 to 1 with higher values indicating better fit

<sup>e</sup> SRMR = Standardized Root Mean Square Residual Entropy values close to 1 are desirable.

<sup>f</sup> The piecewise quadratic growth model was chosen as the final best fit model.

**Table 48 Parameters in a piecewise quadratic growth model of BMI-for-age Z-scores using study sample of SLLCC that has at least 5 BMI measurements from age 7 to 16**

	Estimate	Standard Error	p-value
<b>Intercept</b>			
BMI Z-score at age 7	-0.022	0.002	<0.000
<b>Means (age 7 to 12)</b>			
Slope – S1	0.137	0.001	<0.000
Quadratic trend – Q1	-0.014	<0.000	<0.000
<b>Means (age 13 to 16)</b>			
Slope – S2	-0.119	0.001	<0.000
Quadratic trend – Q2	0.008	<0.000	<0.000
<b>Effect of covariates</b>			
Female gender on intercept	-0.246	0.003	<0.000
<b>Interaction terms</b>			
Q1 with S1	-0.023	<0.000	<0.000
S2 with S1	-0.038	<0.000	<0.000
S2 with Q1	0.004	<0.000	<0.000
Q2 with S1	0.003	<0.000	<0.000
Q2 with Q1	0.000	<0.000	<0.000
Q2 with S2	-0.027	<0.000	<0.000
<b>Variances</b>			
Intercept	1.903	0.003	<0.000
S1	0.141	0.001	<0.000
Q1	0.004	<0.000	<0.000
S2	0.140	0.001	<0.000
Q2	0.007	<0.000	<0.000

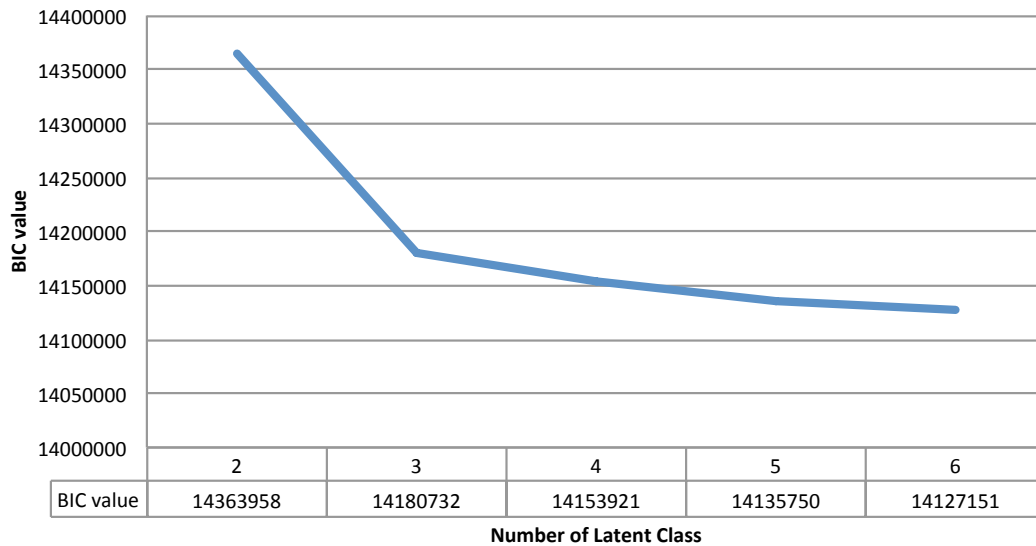
Notes:

SLLCC consists of an extensive individual-level dataset of repeatedly measured anthropometric data, from about 2.7 million students born between 1973 to 2003, collected through routine annual school-based health screening in Singapore from 1990 to 2011.

### 6.3.3 Growth Mixture Models

The aim in using latent growth mixture modelling techniques was to uncover unobserved heterogeneity in a population and to find substantively meaningful groups of students that were similar in their measured BMI growth trajectories (148). Therefore, in order to determine the appropriate number of trajectory groups and trajectory shape for each group, we fitted five latent class growth mixture models (LCGMM), with no covariates, consecutively increasing the number of specified groups or classes.

Figure 28 described the model fit indices (BIC values) and Table 10 provided information on the class counts and proportions for each of the estimated LCGMM.

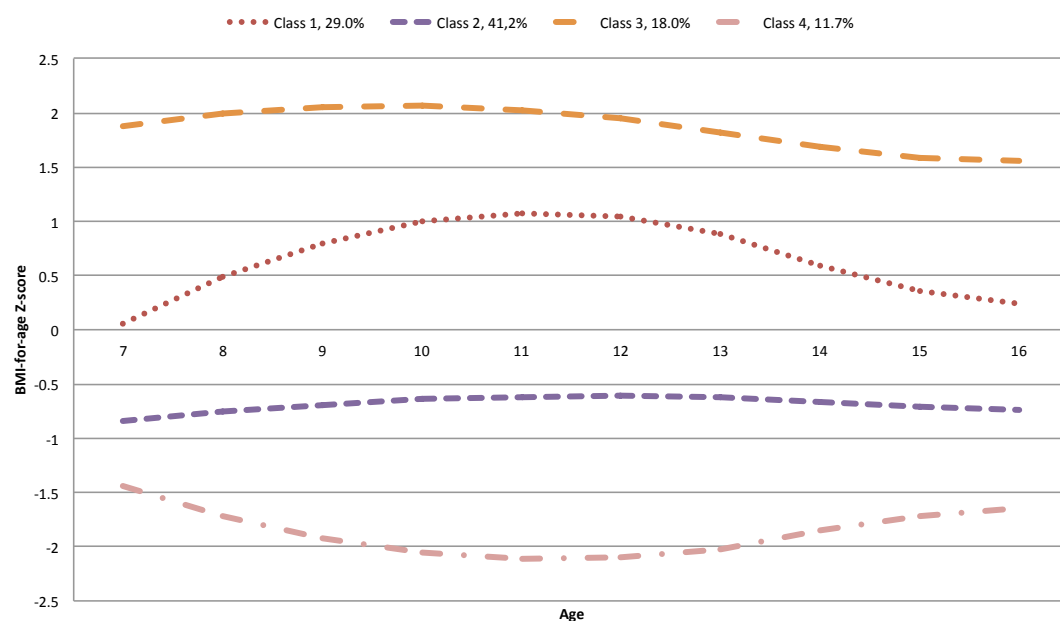


**Figure 28 Plot of BIC values versus number of class in a latent class growth mixture model of BMI-for-age Z-scores in the study sample of SLLCC that has at least 5 BMI measurements from age 7 to 16**

**Table 49 Class counts and proportions of estimated latent class growth mixture models using the study sample of SLLCC that has at least 5 BMI measurements from age 7 to 16**

Class counts (proportions)					
Class	Two-class model	Three-class model	Four-class model	Five-class model	Six-class model
1	33,311 (0.0329)	397,481 (0.392)	294,134 (0.290)	315,062 (0.311)	30,223 (0.030)
2	980,004 (0.967)	205,565 (0.203)	417,928 (0.412)	418,469 (0.413)	412,365 (0.407)
3		410,269 (0.409)	182,539 (0.180)	32,729 (0.032)	313,180 (0.309)
4			118,712 (0.117)	117,154 (0.116)	14,667 (0.014)
5				129,900 (0.128)	110,769 (0.109)
6					132,109 (0.130)

Model fit indices suggested that there were four distinct latent trajectory groups (four classes), given that BIC values started to level from that point (Figure 28). The five-class and six-class models were rejected given presence of classes with very small number of class members and proportions (about 3% and 1%)(Table 49). Furthermore, the four latent growth trajectories were interpretable in context of the conventional BMI categories of underweight, normal weight, overweight and obese in accordance to WHO BMI-for-age Z-score cut-offs (Table 33). Classification quality was modest with entropy value at 0.60.



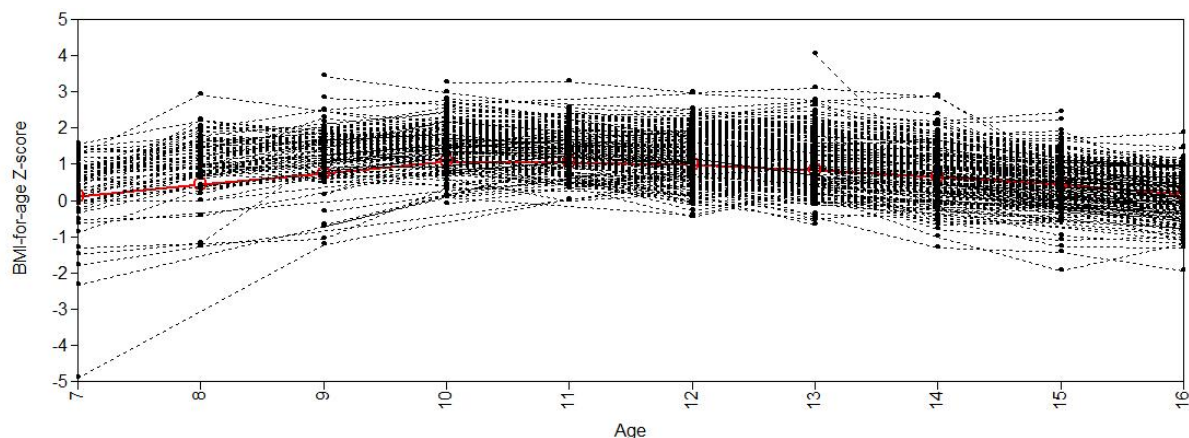
**Figure 29 Best fitted latent class growth mixture model of 4 BMI-for-age Z-score trajectory classes in the study sample of SLLCC that has at least 5 BMI measurements from age 7 to 16**



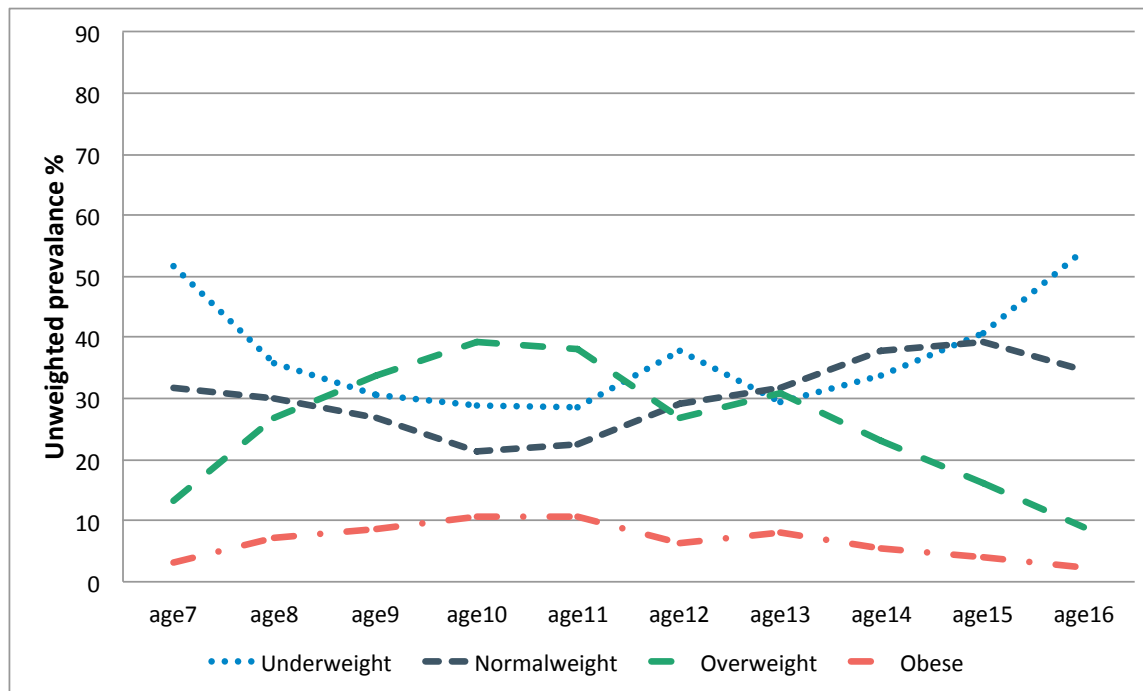
**Table 50 Summary results of the best fitted latent class growth mixture model of 4 BMI-for-age Z-score trajectory classes in the study sample of SLLCC that has at least 5 BMI measurements from age 7 to 16**

Class	BMI-for-age Z-score trajectory groups	Intercept (S.E)	Slope (S.E)	Quadratic (S.E)	Proportion
1	Pubertal-only overweight (PO)	0.055 (0.016)	0.491 (0.005)	-0.059 (0.000)	29.0%
2	Normal-Underweight (NU)	-0.846 (0.005)	0.098 (0.002)	-0.010 (0.000)	41.2%
3	Consistently obese (OB)	1.880 (0.016)	0.132 (0.002)	-0.024 (0.000)	18.0%
4	Consistently underweight (UW)	-1.441 (0.006)	-0.308 (0.003)	0.035 (0.000)	11.7%

The “Pubertal-Only Overweight” (PO) trajectory group (membership: 29.0%) was characterised by a steadily increasing BMI from being normal weight (BMI: 18.5 to <25 kg/m<sup>2</sup>) at age 7 to becoming overweight (BMI: 25 to <30 kg/m<sup>2</sup>) between ages 10 to 13 (corresponding to Tanner stage two/three). Subsequently after puberty, BMI would likely decline to normal weight by age 16 (Figure 30). Within the class, almost 40% of the students were overweight and 10% obese by age 10. While the prevalence of overweight declined over time, the level of obesity did not (Figure 31).

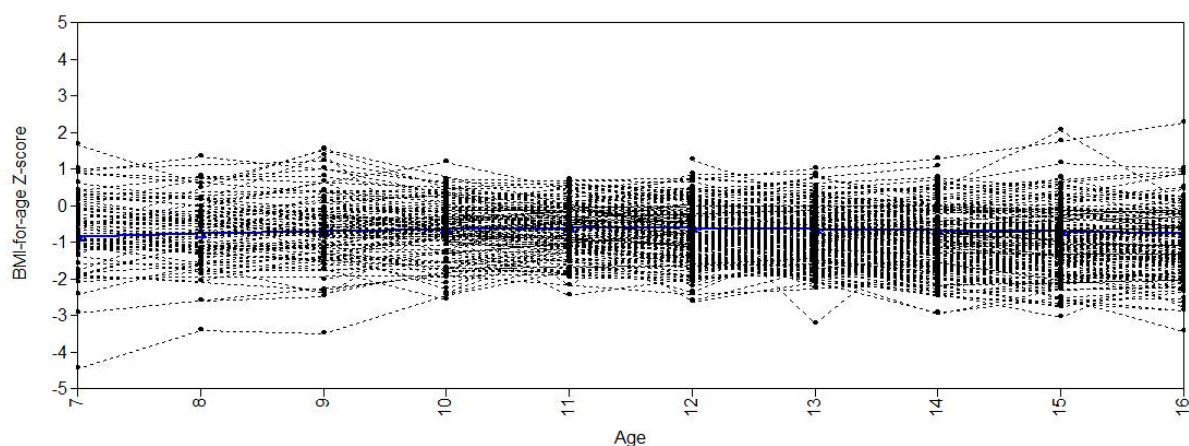


**Figure 30 Random subset of students in the "Pubertal-Only Overweight" trajectory group (class 1) in the best fitted 4-class latent class growth mixture model in the study sample of SLLCC that has at least 5 BMI measurements from age 7 to 16**

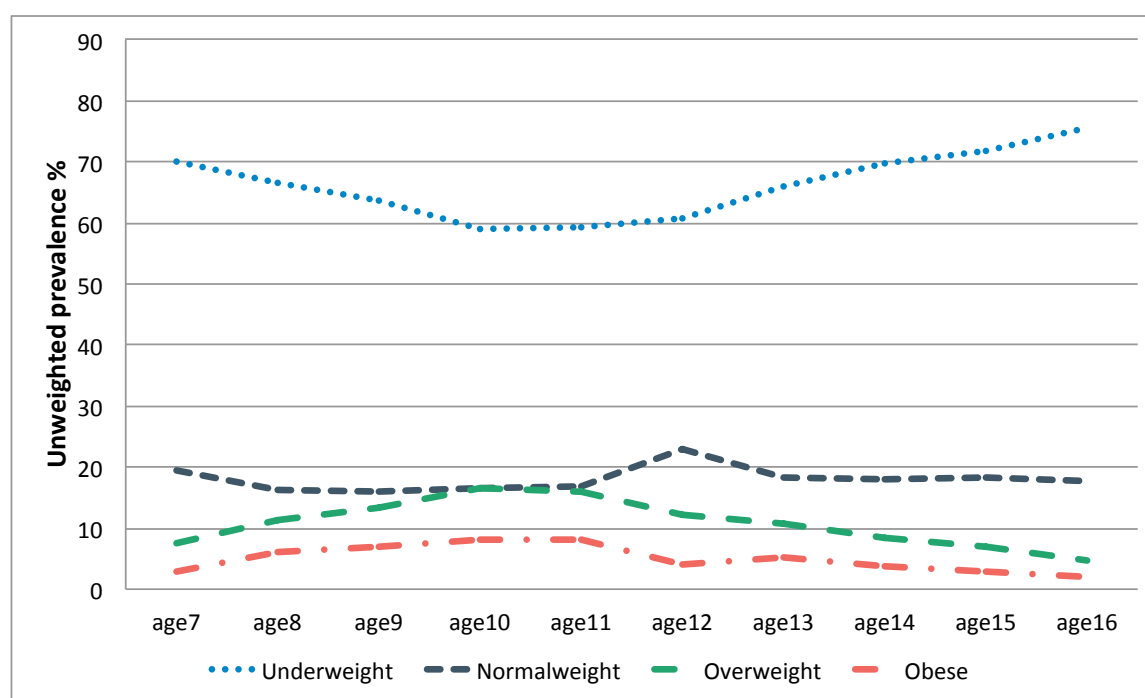


**Figure 31 Pubertal-Only Overweight trajectory group: within-class BMI weight classification prevalence**

The “Normal-Underweight” (NU) trajectory group (membership: 41.2%) was characterised by an average trajectory that remained in the normal weight range (BMI: 18.5 to  $<25 \text{ kg/m}^2$ ) through ages 7 to 16 (Figure 32). Some members of this group may become underweight or classified as Grade 1 Thinness (BMI: 17 to  $<18.5 \text{ kg/m}^2$ ). In fact, it seemed that about 60% to 70% proportion of the students remained underweight through till age 16 (Figure 33).



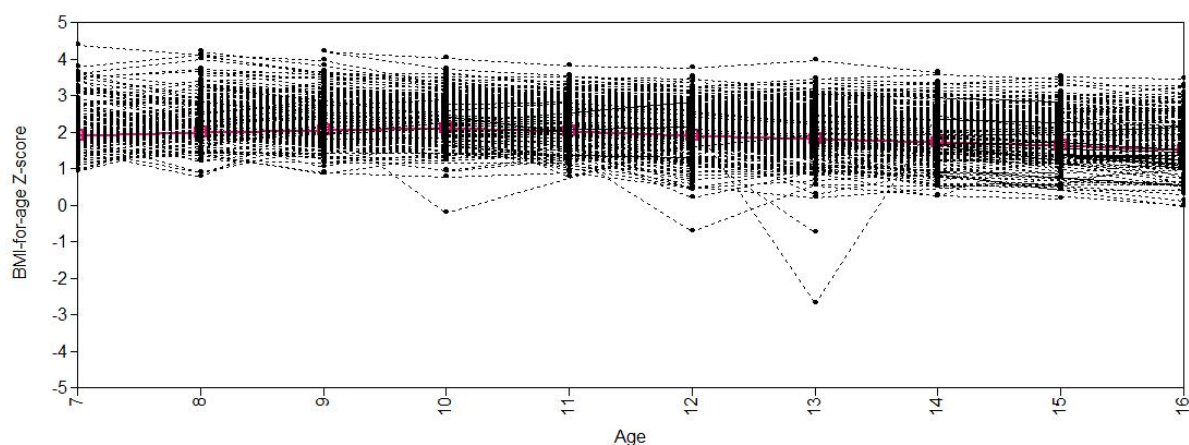
**Figure 32** Random subset of students in the "Normal-Underweight" trajectory group (class 2) in the best fitted 4-class latent class growth mixture model in the study sample of SLLCC that has at least 5 BMI measurements from age 7 to 16



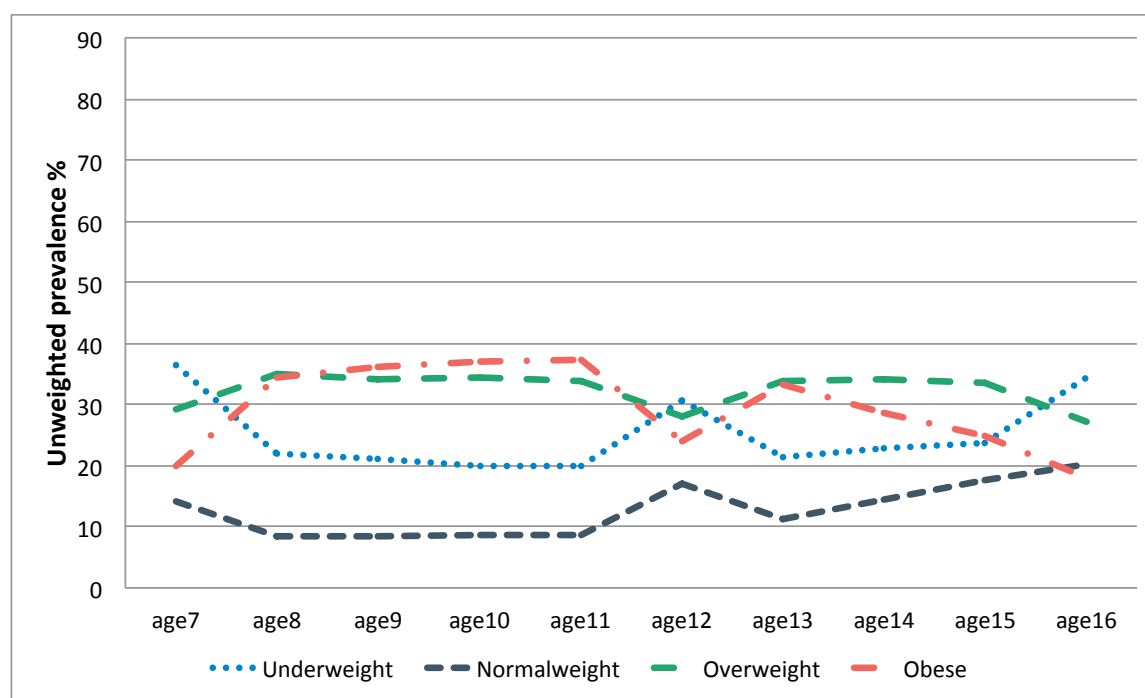
**Figure 33** Normal-Underweight trajectory group: within-class BMI weight classification prevalence

The “Consistently Obese” (OB) trajectory group (membership: 18.0%) was defined by a (slightly concave downwards) curvilinear average trajectory that started in the obese BMI range at age 7 (BMI:  $>30 \text{ kg/m}^2$ ) and remained obese until age 16 (Figure 34). Within-class analysis

revealed that 50% of students in this group were already overweight/obese at age 7, increasing to about 75% by age 8. Prevalence of overweight and obesity continued to plateau, albeit still at high levels, as students progress through primary and secondary schooling, with dips in obesity rates at age 12 and 16 (Figure 35).

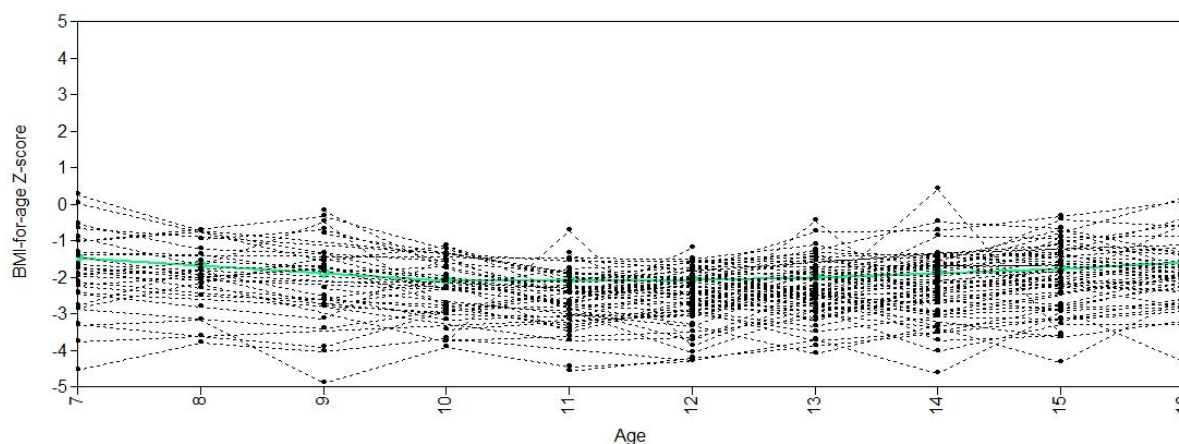


**Figure 34 Random subset of students in the "Consistently Obese" trajectory group (class 3) in the best fitted 4-class latent class growth mixture model in the study sample of SLLCC that has at least 5 BMI measurements from age 7 to 16**

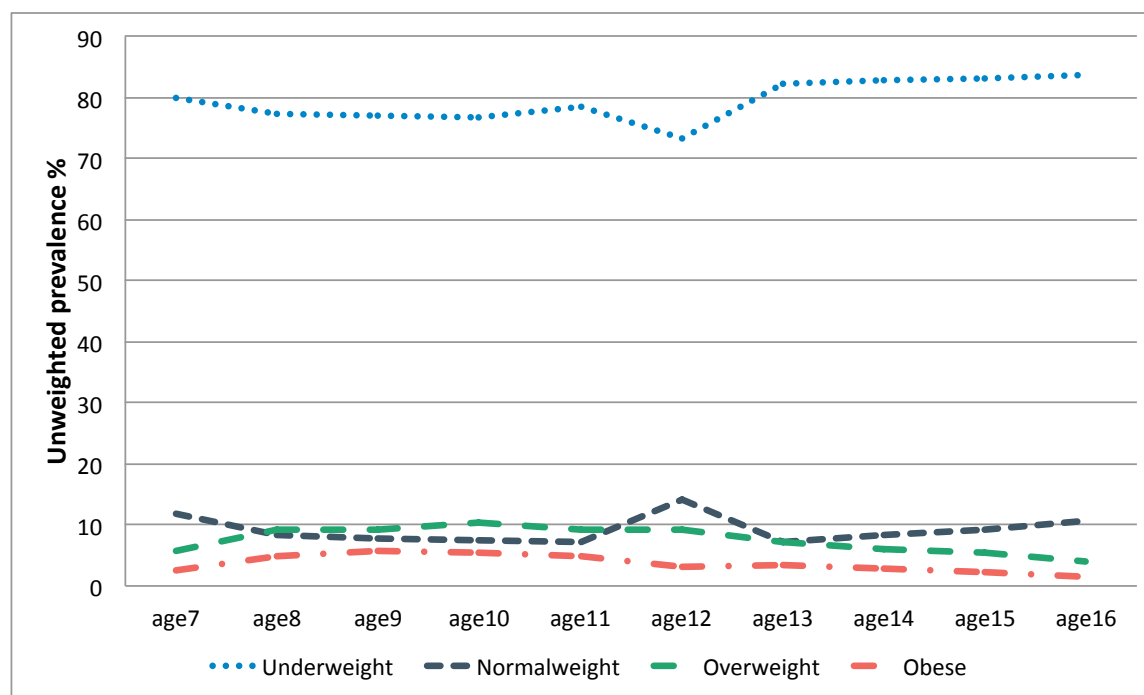


**Figure 35 Consistently Obese trajectory group: within-class BMI weight classification prevalence**

The “Consistently Underweight” (UW) trajectory group (membership: 11.7%) was defined by an average flat trajectory (Figure 36) across all ages. Within this class, about 80% to 85% of students were underweight from the onset (Figure 37).



**Figure 36** Random subset of students in the "Consistently Underweight" trajectory group (class 4) in the best fitted 4-class latent class growth mixture model in the study sample of SLLCC that has at least 5 BMI measurements from age 7 to 16



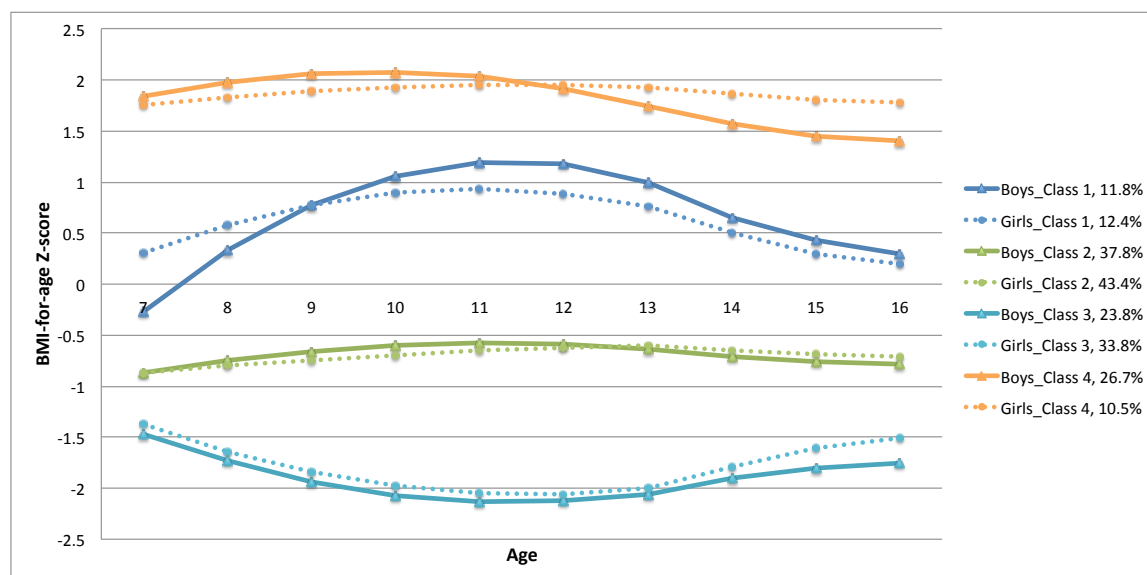
**Figure 37** Consistently Underweight trajectory group: within-class BMI weight classification prevalence

The summary of results for the four-class trajectories model is presented in Table 50. Average posterior probability of group membership for each of the four trajectory groups were from 0.70 to 0.78 (Table 51). Patterns of growth trajectories were also found to differ between males and females, so separate analyses were conducted. In the PO trajectory group, boys had a steeper increase from age 7 to 10 but girls had a higher initial mean BMI Z-score at age 7. Not many differences were observed for the NU trajectory group. For the OB trajectory group, boys experienced higher fluctuations in BMI than girls, with the latter recording a higher BMI Z-score at age 16. Interestingly, boys ended up being more underweight on average than girls in the UW trajectory group (Figure 38)

Within all classes, the mean BMI Z-score for girls were generally lower than boys (Figure 39, Figure 40, Figure 41 and Figure 42). Table 52 summarises the characteristics of members in each of the 4 class trajectories. There were no significant differences in the heterogeneity of gender and racial group make up between the four trajectories and with the entire cohort.

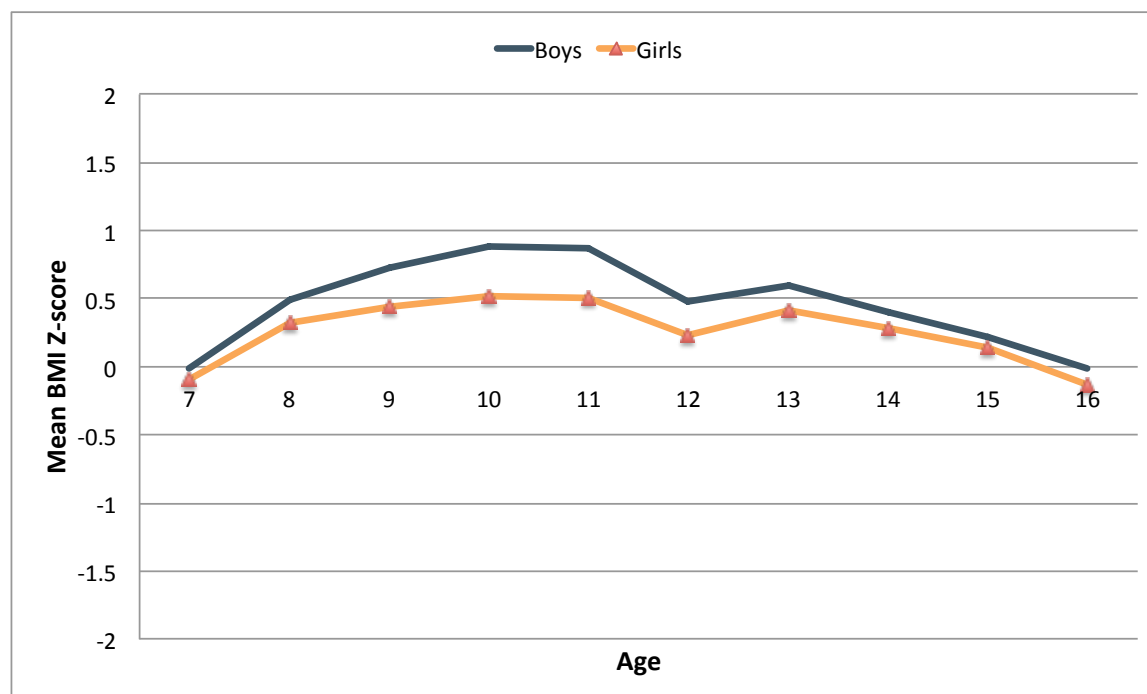
**Table 51 Average latent class probabilities for the most likely latent class membership (row) by latent class (column) in the best fitted 4-class latent class growth mixture model in the study sample of SLLCC that has at least 5 BMI measurements from age 7 to 16**

	Class 1	Class 2	Class 3	Class 4
1	<b>0.707</b>	0.135	0.158	0.000
2	0.112	<b>0.784</b>	0.011	0.093
3	0.214	0.16	<b>0.771</b>	0.000
4	0.000	0.216	0.000	<b>0.784</b>

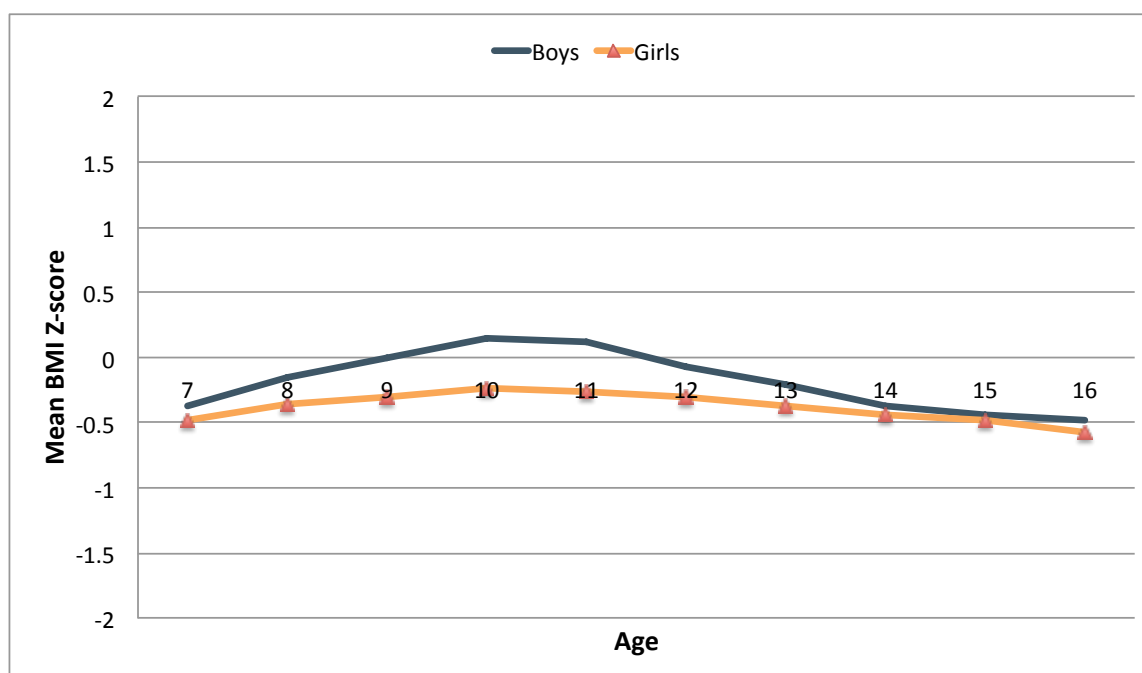


Note: These are separate sex-specific LCGMM combined in a single graph.

**Figure 38 Gender differences in the best-fitted 4-class latent class growth mixture model in the study sample of SLLCC that has at least 5 BMI measurements from age 7 to 16**



**Figure 39 Mean BMI Z-scores of boys and girls in the Pubertal-Only Overweight trajectory group of the study sample of SLLCC that has at least 5 BMI measurements from age 7 to 16**

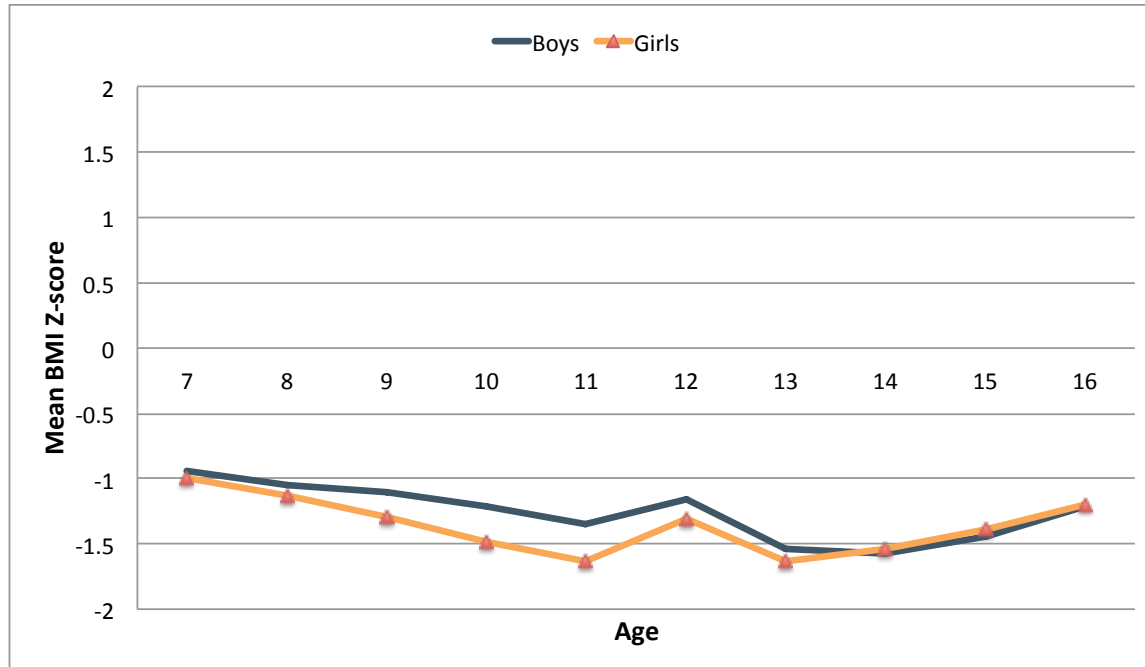


**Figure 40 Mean BMI Z-scores of boys and girls in the Normal-Underweight trajectory group of the study sample of SLLCC that has at least 5 BMI measurements from age 7 to 16**



**Figure 41 Mean BMI Z-scores of boys and girls in the Consistently Obese trajectory group of the study sample of SLLCC that has at least 5 BMI measurements from age 7 to 16**





**Figure 42** Mean BMI Z-scores of boys and girls in the Consistently Underweight trajectory group of the study sample of SLLCC that has at least 5 BMI measurements from age 7 to 16

**Table 52** Characteristics of students in the 4-class trajectories of the best fitted latent class growth mixture model using study sample of SLLCC that has at least 5 BMI measurements from age 7 to 16

	Class 1: PO trajectory		Class 2: NU trajectory		Class 3: UW trajectory		Class 4: OB trajectory	
Gender	Boys	Girls	Boys	Girls	Boys	Girls	Boys	Girls
n	125,727	164,094	199,381	209,845	62,258	60,178	140,759	51,070
%	11.80%	12.40%	37.80%	43.40%	23.80%	33.80%	26.70%	10.50%
Intercept	-0.271	0.306	-0.868	-0.868	-1.466	-1.376	1.838	1.754
Slope	0.676	0.317	0.137	0.073	-0.303	-0.298	0.177	0.09
Quadratic	-0.077	-0.04	-0.016	-0.005	0.034	0.032	-0.032	-0.01
Race group (%)	Class 1: PO trajectory		Class 2: NU trajectory		Class 3: UW trajectory		Class 4: OB trajectory	
Chinese	73.6%		73.0%		70.8%		71.5%	
Malay	13.1%		13.9%		15.1%		14.2%	
Eurasian	0.3%		0.3%		0.4%		0.4%	
Indonesian	2.6%		2.7%		3.1%		3.2%	
Indian	7.5%		7.3%		8.2%		8.6%	
Others	2.9%		2.8%		2.4%		2.1%	

### 6.3.4 Missing data

Given that the SLLCC was derived from record linkages of two routinely conducted national health screening programs among schools, it was not surprising to find a relatively high proportion of missingness in the BMI Z-score variables (Table 53). Since there were no obvious reasons for the incompleteness of the datasets, the assumption of missing at random were made for this study. Percentage-missing values in the four latent trajectories were also found to have no significant differences with that of the study cohort at all ages except for a slightly lower percentage-missing in BMI measurements at age 16 in the NU trajectory group as compared than the overall (Table 54).

**Table 53 Missing values in study sample of SLLCC with at least 5 BMI measurements from age 7 to 16**

Variable	Missing (n)	Total (n)	Missing (%)
id	0	1,013,325	0
BMI Z-score at age 7	366,120	1,013,325	36.13
BMI Z-score at age 8	371,651	1,013,325	36.68
BMI Z-score at age 9	333,325	1,013,325	32.89
BMI Z-score at age 10	300,060	1,013,325	29.61
BMI Z-score at age 11	261,306	1,013,325	25.79
BMI Z-score at age 12	230,477	1,013,325	22.74
BMI Z-score at age 13	300,720	1,013,325	29.68
BMI Z-score at age 14	330,127	1,013,325	32.58
BMI Z-score at age 15	365,575	1,013,325	36.08
BMI Z-score at age 16	461,340	1,013,325	45.53
Number of BMI Z-scores	0	1,013,325	0
Race	0	1,013,325	0
Gender	0	1,013,325	0

**Table 54 Missing BMI Z-score values at each age in the best fitted 4-class latent class growth mixture model in the study sample of SLLCC that has at least 5 BMI measurements from age 7 to 16**

% Missing BMI Z-score values at each age										
Class	7	8	9	10	11	12	13	14	15	16
<b>PO trajectory</b>	38%	37%	32%	28%	24%	22%	29%	33%	37%	10%
<b>NU trajectory</b>	35%	37%	34%	33%	28%	25%	29%	30%	32%	8%
<b>UW trajectory</b>	37%	34%	28%	24%	22%	19%	32%	37%	42%	23%
<b>OB trajectory</b>	36%	42%	37%	31%	25%	19%	29%	34%	40%	22%
<b>All</b>	36%	37%	33%	30%	26%	23%	30%	33%	36%	13%

Particularly for the within-class analysis of the four latent growth trajectories identified, caution should be taken in the interpretation of weight prevalence percentages given that the denominator might have been underestimated due to proportion of missing values at each time point measurement.

## 6.4 Discussion

In this study of 1,013,325 school-age children in Singapore, who had at least five time point measurements of weight and height between age 7 and 16, results suggested that there were four latent growth trajectories - “Puberty-Only Overweight” (PO), “Normal-Underweight” (NU), “Consistently Obese” (OB) and “Consistently Underweight” (UW). The only available independent variables of the participants in the data sets were gender and race groups. No outcome variables were available for further investigation of the impact of being in the respective developmental trajectories.

The NU trajectory could be considered the most favourable group from a public health perspective though it only represented about 41.2% of the total cohort. The next largest group of students were part of the PO trajectory (29.0%), which was characterised by an initial increase in BMI from age 7 and becoming overweight during their puberty period. Subsequently, these students lost weight and by age 15, 80% of them were in the normal weight and under weight bands. Attention should be paid to those falling within the OB and UW trajectories, representing 18% and 11.7% of the cohort respectively, particularly for the former as there is strong evidence of tracking of obesity from childhood to adulthood (55, 61). No significant differences in the heterogeneity of gender and racial group make up between the four trajectories and with the entire cohort could be detected.

Before this study, there have been no other studies using LCGMM research methodology conducted on Singaporean children and adolescents (age 7 to 16) using routine school-based health screening data thus it would be only possible to draw inferences on the potential health implications of the trajectories identified in Singapore from findings of studies predominately conducted in US, Canada and Europe. As a note to the reader of this thesis, this Chapter only focussed on identifying the latent trajectories and the next Chapter applies the same methodology on a subset of the SLLCC cohort that had been linked with the National Health Survey 2010. This allows the latent trajectories to be modelled as a determinant of future health outcomes.

In Canada, three class trajectories have been identified in a representative sample of children for whom BMI data were available for at least 5 time points ( $n=1,957$ ) (260). This study used data from birth registries for the Quebec Longitudinal Study of Child Development,

spanning 9 time points within the first 8 years of children's lives. The trajectories were: an atypically elevated and rising BMI trajectory (4.5%) and 2 groups of children with relatively stable BMI trajectories throughout childhood: a moderate group (41.0%) and a low-stable group (54.5%) (260).

In a US study with seven years (1997–2003) of body mass index (BMI) data derived from the National Longitudinal Survey of Youth 1997 (NLSY97), four subgroups with distinctive developmental trajectories have been identified: 'normal weight', 'overweight', 'late adulthood obesity' and 'early adulthood obesity' (26). Males, Blacks and those born later had higher odds of being in the three latter groups. A higher level of education and greater number of years married flattened the trajectory within each group (26). A rising trend was observed in all four trajectories identified in the NLSY97, whereas the trajectories in Singapore were more or less consistent throughout except for the PO trajectory. The prevalence of most health outcomes in the NLSY97 study was lowest in the normal weight group, somewhat greater in the overweight group, greater again in the late adulthood obesity group and highest in the early adult obesity group.

In a European study, when data from 12,050 subjects of 8 European birth cohorts on asthma and allergies were combined, researchers were able to identify three growth trajectory classes: a normative growth class, a class with early rapid growth up to 2 years of age, and a class with persistent rapid growth up to 6 years of age growth (261). In terms of the differential later-life outcomes based on membership in different trajectories, the study also found that children with a rapid BMI-SDS gain in the first 2 years of life (class 2 and 3) had a higher risk

for incident asthma than children with a less pronounced weight gain slope in early childhood (261).

### **Addressing underweight in children**

More often than not, the underlying prevalence of underweight can be easily overlooked given the attention on obesity trends. A child's body responds to malnutrition in two ways that can be measured by anthropometry: a deceleration or cessation of growth, which over the long term results in low height-for-age or stunting; and body wasting, which is a short-term response to inadequate intakes, and commonly assessed by weight relative to height (248). Height-for-age and weight-for-height thus discriminate between different biological processes, unlike weight-for-age, which could be low because of stunting (short stature) and/or wasting (recent weight loss) (248). In the case of this study, the use of BMI-for-age classification of weight status would not have been able to discriminate between short-term and long-term forms of malnutrition or obesity. Ideally, it would be appropriate to use height-for-age and weight-for-height measurements as the indicators of choice for health screening (248), unfortunately height information was not available for all subjects in the Singaporean dataset (only calculated BMI values were provided by the Ministry of Education's TAF datasets).

In any case, another key finding of this study that may warrant additional investigation is the identification of the UW trajectory group that comprised 11.7% of the cohort and it should not be overlooked that about 80% of students in this class were underweight from the onset and remained underweight. At the same time, about 60% to 70% proportion of the students was also underweight in the largest NU trajectory group (41.2% of cohort).

### **Effect of education transition from primary to secondary schooling**

In terms of findings to support whether educational transition from primary schools to secondary schools account for shifts in trajectories, and whether these patterns differ for boys and girls, this study was able to successfully fit a piecewise quadratic growth model of the rate of change of BMI Z-scores during two distinct childhood and adolescent stages of life, even though the two development phases - ages 7 to 12 during primary schooling and ages 13 to 16 during secondary schooling were determined *a priori*. The findings suggested a mean BMI Z-score of -0.022 at age 7, within normal weight range of (BMI: 18.5 to <25 kg/m<sup>2</sup> at 18 years). The rate of change (slope factor) in the first six years of primary schooling was found to be increasing at 0.137 standard deviation of BMI Z-score unit annually with a slight plateau at about age 12 to 13. Subsequently, there is a statistically significant decline of -0.119 standard deviation BMI Z-score units until age 16. Being female was found to have a protective effect of lowering mean BMI at age 7 ( $p < 0.05$ ). One other consideration is that if all students had started primary and secondary schooling at the same age, then the observed effect might potentially be confounded by age. In developing the SLLCC, age as a variable was derived based on the reported academic level during health examinations (Table 30). Ideally, age could be calculated based on birth date and date of examination, but unfortunately, the latter was not available in the SHS and TAF data sources. Therefore, further research is required to adjust for additional confounders of the influence of the transition between primary and secondary schooling.

Given that the dataset only included gender and racial groups as a covariate, there were limited options to address the aetiology of the anthropometric trends detected in this study.

However for this current study, a number of possible explanatory factors may be postulated. These included consideration of:

### **1. Genetic predisposition**

There is a growing pool of evidence involving large childhood populations investigating the effect of known adult genetic determinants of BMI on childhood growth trajectory.

Researchers have shown that the genetic effect begins very early in life, which is consistent with the life course epidemiology hypotheses – the determinants of adult susceptibility to obesity begin in early childhood and develop over the life course (262). Certain genetic variants could also affect features of the growth trajectory and shape key developmental milestones, including the adiposity peak (263), adiposity rebound, and onset of puberty between 10 and 13 years (264, 265).

In Singapore, associations between nine previously reported FTO (fat mass and obesity-related gene) with obesity and type 2 diabetes were identified in a sub-cohort of the 1998 Singapore National Health Survey and the Singapore Malay Eye Study (212). This confirmed that FTO variants common among European populations were associated with obesity in ethnic Chinese and Malays in Singapore. In relation to this study, hypothetically, if access to genotyping of the parents of students were available, one could attempt to determine the heritability of the FTO gene and epigenetic effects of maternal diet, in addition to epigenetic markers at birth as a function of foetal growth and subsequently over development and its effect on childhood obesity. Unfortunately, data in SLLCC do not yet include any parental genetic or phenotypic information at this point.



Some studies on obese children and their parents had also shown a strong negative correlation with age at onset of obesity with severity at age 7; however, it was not clear whether the relationship between parental BMI and severity of obesity in their children was due to genetic or environmental factors (47). It was interesting however, to note that the correlation between parental BMI and severity of obesity for their children at age 15 became more pronounced, suggesting that genetic factors may dominate later in life with decreasing parental impact on daily life. Several twin studies in children confirmed that genetic factors influencing weight, BMI and body size became more apparent with age (42-45) despite the “obesogenic” environment (46).

## **2. Social economic positions**

While this analysis did not set out to explore how socially patterned exposures during childhood and adolescence might influence adult disease risk, recent findings from studies of trajectories of family income during childhood suggest that trajectories that ended with a higher proportion of children in low-income families showed greater adiposity at age 15, while the trajectories ending with a lower proportion of children in low-income families showed less adiposity. Conversely, upwardly mobile children and those with consistently adequate incomes had similar and more positive outcomes relative to the most disadvantaged trajectories. This suggested that changes in socioeconomic status during childhood may influence adiposity in adolescence and that promoting upward socioeconomic mobility among disadvantaged families may have a positive impact on obesity-related outcomes in adolescence (254).

Relevant SES factors such as parent's employment, household income, parent's education would be useful to include in any future analysis of similar design to this study.

### **3. Individual and family behavioural factors**

Understanding why some people exercise more than others is a complex social and psychological challenge, and the challenge is even greater when explaining physical activity in children and adolescents. Having knowledge about the general prevalence of the school-age population engaging in physical activity is fundamental, however, in order to support interventions aimed at increasing the level of physical activity at the community or neighbourhood level, it becomes necessary to have a better understanding of the relationships between social determinants of health, physical activity and where people live.

More importantly, the roles of childhood dietary patterns that are high in energy-dense, high-fat and low-fibre foods have been strongly suggested to predispose young people to later overweight and obesity (266). It also remains critical to combine diet and physical activity interventions, which may be more effective in preventing children becoming overweight in the long term (267). In Singapore, prospective studies on childhood and adolescent nutrition are scarce, with the first and only to-date school health survey (cross-sectional design) conducted on Secondary 1 to Secondary 4 students (ages 13-16 years old) in 2006. The survey revealed that only 40% and 46% of the students consumed the daily recommended 2 servings of fruit and vegetables daily respectively. 29% of them consumed sweetened drinks more than once a day and 52% of them consumed deep fried food more than twice a week (225).

The effect of family dynamics and time use at home, particularly, mothers' employment patterns may be more closely associated with children's BMI than fathers' through their greater association with both the quality and quantity of children's time. Understanding the developmental trajectories of children's BMI and how parents' employment patterns relate to these growth trajectories could also potentially illuminate opportunities for clinical and policy interventions (268).

#### **4. School level factors**

Academic performance in schools has the potential to alter the trajectory of childhood weight gain and subsequent adolescent outcomes. Previous studies have reported that the odds of membership in a persistently overweight class were significantly reduced among those with a higher average grade in high school (174). The evidence also suggested that individual resources and other collective social capital operating in the school setting can attenuate the risks for obesity and overweight even among those from a lower social economic status (313). At the time of the study, there was no obvious access to individual level academic performance in schools in Singapore.

Policymakers, researchers and media have always promoted the school as a logical strategic setting for implementing nutrition policies aiming at promotion of healthy diet and tackling childhood obesity. However, a recent systematic review concluded that the current evidence of effectiveness were limited, and no studies of cost-effectiveness were identified, although its included studies were mainly based on research in US and European settings and

may not be directly applicable in Asian contexts (269). In Singapore, the impact of school food policies on BMI has not yet been evaluated.

Finally, even given the small geographical area of Singapore, it will be important to consider whether the vast set of economic and demographic changes occurring over the past four decades have created a new set of circumstances that may increase the likelihood of childhood overweight and obesity in Singaporeans.

## **6.5 Strengths and limitations**

The main limitation of this analysis was the lack of information on the study subjects, which did not provide much explanatory power to interpret the findings. While several interesting patterns of growth change were identified, it was not possible to examine the association or causality between predictors and these patterns. Early life determinants on childhood overweight and obesity under 5 years old that were not explored include genetics, maternal factors, birth weight, infant size and growth, infant feeding, sleep duration, family, physical activity and sedentary behaviour, society and built environment, which could all potentially have an effect on childhood obesity to different extents (41).

Given that this study population was a sub-set of the Singapore Longitudinal and Life Course Cohort (SLLCC) that was retrospectively constructed based on record linkages of individual-level anthropometric examinations from two separate national health screening programs, the analysis had to deal with similarly high proportion of missing values at each of the 10 time point measurements of height and weight. Ideally, additional sensitivity analysis and the

use of techniques such as Bayesian multiple imputation to address missing values could have been undertaken (270). In this study, data missingness was handled using full information maximum likelihood under the assumption of missing at random.

Another limitation is that this study did not consider cohort effects on latent growth trajectories, which is a widely observed phenomenon that more recently born cohorts had higher BMIs when compared at the same age with older cohorts (271). Age, period and cohort effects were similarly detected in an earlier analysis of this thesis (Chapter 5). Without access to weight at birth, the study could not take into account any potential effect of post-natal catch up growth or adjust for the tendency of low birth weight infants to have childhood overweight and obesity or the continued effect that neonatal morbidity exerts on height and weight development from birth to age 12 years (272).

To date, Singaporean longitudinal studies are few (150-153) and thus, this study was the first attempt to utilise routine data, not collected in a trial or under research protocol guidance, as a valuable source of longitudinal information on childhood and adolescent BMI change over time. Previously, the main sources of information on obesity-related trends were the National Health Surveys, which were conducted every six years and only restricted to monitoring adult growth at a single point in time.

This study has several strengths. Firstly, the study analyses were made on 1,013,325 school-age children, who had at least five time point measurements of weight and height between age 7 and 16. Secondly, by not using interviews and respondent recall, there is no

respondent burden or recall or reporting errors (except those that cannot be validated in terms of inaccurate data entry during health screening as the data collected was not intended for research at the point of examination). Thirdly, since the National Registration Act of 1965 (178), all Singapore citizens and permanent residents were issued a unique NRIC number. This promised great potential in the establishing individual-level linkages to several other existing national datasets such as the Singapore Census of Population, Household Surveys, both of which are rich sources of revealing additional demographic, economic, household, travel characteristics of SLLCC subjects.

In terms of methodological strengths, the use of internationally adopted WHO BMI Z-scores cut-offs would permit comparison with studies in other settings and countries. The application of latent class growth model strategies to explore over two decades of longitudinal childhood BMI Z-score data was also considered a first in the Singapore context, to the best of my knowledge. This study employed latent class analysis strategies that initially estimated a single underlying trajectory in the study population, then compared separate models for each group (gender and ethnicity) and finally, testing for the existence of multiple developmental trajectories/pathways within the whole study population using latent class growth mixture models. This strategy proved to be useful and advantageous to better understand latent changes in the childhood and adolescent obesity development between 1990 and 2011.

## **6.6 Conclusions**

In conclusion, recognising the public health imperatives is important in this research. Identifying individuals as belonging to groups of distinct BMI trajectory characteristics early

may provide both the individuals themselves and their health-care providers' opportunities to initiate early behavioural or other health promotion interventions better tailored to the specific group (25, 26). Between 1990 to 2011, four latent growth trajectories were identified, suggesting that 41.2% of the 1,013,325 study subjects, who had at least five time point measurements of weight and height between ages 7 and 16 were "Normal-Underweight"; 29.0% were overweight during their puberty period but returned to being normal weight by age 16; 11.7% were "Consistently Underweight" and 18% were "Consistently Obese" through out their 10 years of schooling life. Early screening for overweight status and systematic, regular, monitoring of BMI may aid in early identification of those at risk of being in the "Consistently Obese" trajectory group.

The Singapore Longitudinal and Life Course Cohort (SLLCC) is the largest longitudinal cohort of youth (ages 7 to 18) in Singapore to-date. It consists of an extensive individual-level dataset of repeatedly measured anthropometric data, from about 2.7 million students born between 1973 to 2003, collected through routine annual school-based health screening in Singapore from 1990 to 2011. Utilising data from SLLCC, this study identified valuable new information regarding anthropometric developments of children and adolescents and demonstrated the usefulness of routinely collected school based health screening data in understanding the childhood obesity situation in Singapore.

## **Chapter 7: Understanding relationships between childhood and adolescence developmental trajectories with mental health well being in Singapore**

### **Synopsis**

In the systematic review of the evidence of weight change on later health outcome in Chapter Two, one can appreciate the limitations of studies that investigated the impact of earlier growth development on later life outcomes using the differences in weight change between two time points only (in 18 out of 30 included studies). Thus, an attempt was made to establish a longitudinal cohort with repeatedly measured anthropometric changes among Singapore youth in Chapter Three and Chapter Four using routinely collected data.

However, the main challenge in most life course research of this nature is how to make causal inferences with prospective data in which the outcome of interest in later life is the result of the entire trajectory of change in individuals across the life course. In Chapter Six, I hypothesise that BMI changes is not static among school-age children and manage to characterise four latent growth trajectories, for the first time, in the study of obesity aetiology in Singapore. Chapter Five and Six is a demonstration of the potential of the SLLCC to enhance childhood and adolescence obesity research in Singapore.

Bi-directional associations between childhood obesity and depression have been reported in several studies and confirmed by meta-analysis of longitudinal studies (273). However, in the only study in Singapore exploring associations of BMI and mental disorders, the Singapore Mental Health Study (SMHS) did not find any association between overweight/obesity and health-related quality of life in the overall sample, after adjusting for confounding factors (274).



Given that mental well-being data are available in the NHS 2010, this presents as an opportunity for individual-level childhood weight history from the SLLCC to be retrospectively linked to selected respondents of the NHS 2010 so that statistical approaches of latent growth modelling (like in Chapter Six) can be applied, identifying childhood growth trajectories as a determinant for early adulthood psychological distress. Contrary to the earlier SMHS findings that BMI at a single point in time does not associate significantly with health-related quality of life, I hypothesise in Chapter Seven that individuals who exhibit differential trajectories of weight change from age 7 to 16 will have significant differential relative risks of poor mental well-being in later life.

## **7.1 Introduction**

There are serious growing concerns about the rising epidemics of childhood obesity (1, 186) and poor mental health, particularly depression, worldwide (275, 276). Mental and substance use disorders were ranked 5<sup>th</sup> as a leading cause of diseases in the world, in the Global Burden of Disease Study 2010 (277) with mental and substance use disorders accounting for 184 million disability adjusted life years (DALYs) (7.4%) of all DALYs worldwide (278). In 2010, it was estimated that there were about 43 million overweight and obese pre-school children (i.e. 2 standard deviations (SD) above the median WHO standards) in developing and developed countries. In addition, 92 million pre-school children were estimated to be at risk of overweight (185).

The health implications of these global trends are worrying, especially for children and adolescents given that mental disorders commonly occur in the general population, often have an early age-of-onset, and often are associated with significant adverse societal costs (29, 32). Early-onset Major Depressive Disorder (MDD) in particular is found to predict difficulties in subsequent role transitions, including low educational attainment, high risk of teen child-bearing, marital disruption, and unstable employment (279). A meta-analysis has also confirmed that depression is a risk factor for various cardiovascular diseases (including myocardial infarcts, coronary heart disease, cerebrovascular diseases) in general practice populations as well as among community populations (280). Childhood obesity has also been reported as a risk factor for adolescent depression (281).

The very first systematic review of the body of evidence for the hypothesised association between obesity and incidence of depression outcomes found weak evidence. This was mainly because of the small effects among the few prospective cohort studies, as well as limited generalizability as samples consisted mostly of middle-aged to older adults from two populations (Finland and United States). Although cross-sectional studies from the United States consistently showed associations between obesity and prevalence of depression outcomes for women and men pooled, and only for women but not men when analysed separately; whereas cross-sectional studies from other populations consistently failed to show any such associations (281).

The association between depression and obesity was subsequently further investigated by four other meta-analyses a few years later. One meta-analysis of 17 community-based studies with a total of 204,507 participants, found a significant association between depression and

obesity (OR=1.26, CI: 1.17–1.36) (282). All the potential moderators (age, continent of residence, year of publication and differences in measurement methods) did not influence this association, with the exception of gender (282). These findings were consistent with evidence when associations were with abdominal obesity only versus general obesity measured through Body Mass Index (BMI) in the second separate meta-analysis (283). In the latter systematic review of 15 cross-sectional studies, the authors found a moderately strong relationship between abdominal obesity and depression (OR=1.38, CI: 1.22–1.57), which was stronger than that between general obesity and depression as revealed by the former systematic review of community-based studies (OR=1.26) (282).

In both reviews, the association between depression and obesity was more clearly present in females than in males (282, 283), which was already a well-known phenomenon documented in several studies (284, 285). The general consistency in the existing body of evidence for obese women had been partly attributable to stronger associations with psychopathological factors, as well as higher prevalence rates of depression as compared to obese men (286).

Researchers often regard the fact that while cross-sectional evidence is informative, it does not provide sufficient detailed insights into the temporal relationships linking depression and obesity. Evidence is somewhat mixed as to whether depressive symptoms and other negative emotional states may increase risk for adiposity gain and obesity onset within adolescence (287). Longitudinal studies are therefore, essential in providing more information on the direction of the association. In this regard, we highlight the third and fourth notable reviews here. The third was a recent meta-analysis, which specifically examined longitudinally whether overweight and

obesity increase the risk of developing depression and whether depression increases the risk of developing overweight and obesity. The pooled odds ratios from 9 studies examining the effect of depression on obesity over time, confirmed significant bidirectional associations between depression and obesity: obese persons had a 55% increased odds of developing depression over time (OR=1.55, CI: 1.22–1.98), whereas depressed persons had a 58% increased odds of becoming obese (OR=1.58, CI: 1.33–1.87). The association between depression and obesity was also stronger than the association between depression with overweight, reflecting a dose-response gradient for both men and women (273).

These findings were consistent with those of the fourth review of longitudinal studies reporting that children with behaviour problems were at increased risk of future overweight, however, whether this risk was conferred by conduct symptoms, Attention Deficit Hyperactivity Disorder (ADHD) symptoms, or both, was less clear. Like many others, the review found that obese adolescent females are more likely to develop depressive illness in adulthood than their non-obese peers. Conversely, depressed adolescent females, and possibly males, are more likely to become overweight adults than non-depressed adolescents (288). The verdict is clear that the physiological and behavioural changes during adolescence warrant the attention of health practitioners to prevent the onset and continuation of obesity throughout the lifespan (289).

More than 85% of the world's population lives in 153 low-income and middle-income countries (LAMICs), many of which still allocate very scarce financial resources and have grossly inadequate manpower and infrastructure for mental health (290). Although nearly 80% of the 191 countries reviewed by the World Health Organization in 2007 had a mental health policy

or programme (or both) and about 70% have mental health legislation, nearly 70% of countries in Africa and 50% in Southeast Asia spent less than 1% of their health budget on mental health care (290). By contrast, more than 60% of European countries spent more than 5% of their health budget on mental health care. Singapore, a developed economy with 4.3 million population, at the time of the study, allocated 4.5% of its Gross Development Product (GDP) on health, of which 6.1% of the health budget were spent on supporting mental health programs and facilities. This compared well with countries with similar social economic demographics like South Korea (3%), the Netherlands (7%), Sweden (11%), United Kingdom (10%) and the United States (6%) (290).

Over the past 40 years, the epidemiology of mental health disorders in Singapore has evolved considerably and our understanding of the aetiology of the disease has improved with increasing availability of data from national prevention campaigns. In 1978, the Ministry of Health reported 8.4% of the population as suffering from ‘neurosis’. About a decade later, in 1989, a cross-sectional survey of over 3,000 residents estimated a prevalence of 16.6% with ‘minor psychiatric morbidity’ (MPM) with rates for Chinese was (17.4%), Malays (15.1%) and Indians (17.8%) (291). A few years later, the National Mental Health Survey 2004 reported lifetime prevalence of depression to be 5.6% of the population and that of anxiety disorders to be 3.4% (292).

More recently, the prevalence of poor mental health as measured on the General Health Questionnaire (GHQ-12) among Singapore residents aged 18 to 69 was 12.9% in the National Health Survey 2010. A higher proportion of females (14.1%) had poor mental health compared

to males (11.5%). Significant differences among the ethnic groups as compared to 1989 were observed: Indians (11.5%) had the lowest prevalence of poor mental health compared to Malays (13.0%) and Chinese (13.0%). The prevalence of poor mental health was highest among the younger adults aged 18 to 29 years (18.4%) (21).

In 2012, the landmark Singapore Mental Health Study (SMHS) was established as a population-based, cross-sectional, epidemiological study of the mental disorders of the Singapore multi-ethnic adult population. Among the 9116 respondents, 6648 (72.9%) respondents were successfully interviewed (30). The cohort profile and design methodology has been described in more detail elsewhere (293). SMHS revealed a number of meaningful insights and represented the most current epidemiology knowledge base of the mental health situation in Singapore, to-date.

Some of the most relevant findings are reported here. In terms of disease epidemiology, the lifetime and 12-month prevalence estimates for MDD were 5.8% and 2.2%, respectively. The prevalence rates of lifetime and 12-month MDD were significantly different across ethnicity. Lifetime prevalence of MDD was significantly higher among the Indians (8.1%) than among the Chinese (5.5%) and Malays (4.5%) ( $X^2=38.3$ ,  $p<0.0001$ ). 12-month MDD rate among Indians was 4.0% versus 2.0% among the Chinese and Malays ( $X^2=20.4$ ,  $p<0.0001$ ) (294). Women had higher odds than men for having lifetime affective disorders (prevalence of MDD was 7.2% versus 4.3%,  $P<0.0003$ ; dysthymia was 0.5% versus 0.04%,  $P<0.001$ ) (30).

Comparing the 12-month MDD prevalence rate of 2.2% in the multi-racial Singapore population with the 17 countries, which participated in the WHO World Mental Health (WMH) Survey, our 12-month rates were lower than those in developed Western countries (295) and similar to Japan (2.2%).

In terms of age of onset, the highest rates of MDD were found in the youngest age group i.e. in those aged 18 to 34 years. Thereafter, it decreased and levelled off with increasing age. The same applied to those with bipolar disorder. Respondents belonging to the younger age group (18 to 34 years) ( $P < 0.001$ ), those who were separated or divorced ( $P < 0.001$ ), unemployed ( $P = 0.001$ ) or having any chronic physical condition ( $P = 0.003$ ) were more likely to have a comorbid mental disorder. The median age of onset of MDD was 26 with an interquartile range (IQR range) (294)

This compared closely with the mean age-of-onset (28 years) for depression to that reported in the World Mental Health Survey of 28.9 years among their group of developed countries and 27.2 years for developing countries (295).

The SMHS also estimated that 16.3% of the Singapore population reported having multiple chronic medical conditions (MCMC) suffered a lower quality of life than those with one medical illness (0.88 vs. 0.94,  $P < 0.001$ ) and that those of Malay ethnicity had a lower risk of multi-morbidity as compared to Chinese (31). In essence, two important yet potentially modifiable risk factors for MCMC were found: psychiatric disorders and obesity (31).

Given the established comorbidity of obesity and depression, the association between early life anthropometric changes and mental health well-being warrants further exploration. In an earlier study in Singapore, being underweight was associated with both lifetime and 12-month obsessive-compulsive disorder (OCD) and any of the two anxiety disorders (i.e. 12-month generalised-anxiety disorder (GAD) or OCD). Obesity was associated with 12-month alcohol dependence. 1.0% of obese people had 12-month alcohol dependence as compared to 0.3% of the normal BMI group (adjusted OR=8.4) (274).

However, in that analysis, BMI was based on self-reported weight and height at a single point-in-time and did not reflect the life course effects of earlier childhood and adolescent growth development, which had been demonstrated to influence later life health outcomes (26, 27, 251) or risky behaviours (296). The rationale for the latter approach had been shown in developmental psychology (71, 72), where relationships between the different obesity trajectories and psychiatric disorders were specified in a latent growth model framework (73), of which probabilities of group membership may be derived. It may be, for example, that the predictors of being in an “always obese” or “early onset of overweight” group are quite different from the predictors of being in a “becoming obese” or “late onset of overweight” group.

Recently, a “dose-response” relationship between years of duration of obesity with all-cause, cardiovascular, cancer and other-cause mortality (50) and diabetes (51) had been uncovered and with the increasingly early age of onset of obesity in children in Singapore in more recent birth cohorts (findings from Chapter 5), it would be important to know if there is a difference between a child being obese at an earlier age and exposed to a longer sustained period



of high BMI-for-age would predict a poorer mental health in later life. Knowledge of this relationship would contribute to improving prevention strategies that can help delay onset of obesity and to consider duration of obesity when estimating future mental health burden associated with childhood obesity trends in Singapore.

## **7.2 Aim of the study**

Therefore, the aim of this study is to determine whether latent growth trajectories during childhood and adolescence may predict a person's mental health well-being later in life in the Singapore multi-ethnic Asian population context.

## **7.3 Methods**

### **7.3.1 Study cohort**

#### **National Health Survey 2010**

The National Health Survey (NHS) is part of the Ministry of Health's on-going surveillance of the health status of Singapore. It provides regular information on the prevalence of major non-communicable diseases such as diabetes mellitus and hypertension and related risk factors like obesity and smoking from a representative sample of the resident population. The NHS 2010 was the fourth in a series of surveys conducted once every six years to assess and monitor the health of the Singapore population. Data collection procedures had been previously described elsewhere (147) so key aspects and the data collection procedures of the survey are repeated here for the purposes of informing the reader of this thesis. Recently, the NHS also captured information on mental health (21). The 12-item General Health Questionnaire (GHQ-

12) was used to measure mental health. Cut-off for poor mental health was based on an earlier validation study conducted in 2003 (scored larger than 3)(21).

The NHS 2010 covered non-institutionalised Singapore residents (Singapore citizens and permanent residents). The sampling plan followed a multistage design. At the first stage, sampling divisions within close proximity of the designated survey sites were chosen. Dwelling units of each selected sampling division were then stratified by house-type and systematically selected at the second stage. The eventual sample (n=4,337) was representative of the house-type distribution of the whole housing population in Singapore.

### **Singapore Longitudinal and Life Course Cohort**

The Singapore Longitudinal and Life Course Cohort (SLLCC) is the largest longitudinal cohort of youth (ages 7 to 18) in Singapore to-date. It consists of an extensive individual-level dataset of repeatedly measured anthropometric data, from about 2.7 million students born from 1973 to 2003, collected through routine annual school-based health screening in Singapore from 1990 to 2011.

The primary data sources of the SLLCC were the School Health Service (SHS) database from Health Promotion Board (HPB) and the Trim and Fit (TAF) database from the Ministry of Education (MOE). Both datasets captured information routinely collected from an on-going annual health screening dataset of school children in all primary schools (for ages 6 to 12) and 95% of all secondary schools (for ages 13 to 16) in Singapore. Based on procedures described in Chapter Three, a unique random record identifier was allocated to each student NRIC number

(Singapore National Identity Card) so that every record of the same student, regardless of whether his or her data was captured during HPB health screening programme or MOE TAF programme at his or her school, would be linked at the individual level across the different ages that his or her weight/height was recorded during the entire schooling period from age 7 to 16.

### **Study cohort for this analysis**

Briefly, the Ministry of Health, who owned the NHS 2010 data, provided the list of unique identifiers (NRIC numbers) of only NHS 2010 respondents aged 18 to 26 years, to the Health Promotion Board, who owns the SLLCC data sets. The two data sets were then submitted to a third party data vendor who independently linked both data sets by their NRIC numbers and returned the resulting merged set of de-identified records for the purposes of this study.

A total of 519 out of 598 students (86.8%), aged 18 to 26 from the NHS 2010 were matched with the SLLCC data sets. This linked 10 repeated measurements of their childhood and adolescence BMI from when they were at age 7 to 16 to their later life health outcomes in 2010. Older respondents of the NHS 2010 were not included in this study as the oldest birth cohort in the SLLCC that had a complete set of BMI measurements from age 7 to 16 was born in 1984, thus they would be 26 years of age in 2010 (at the time of the NHS)

### **7.3.2 Mental health measurement**

The primary health outcome is psychological distress as measured by the General Health Questionnaire (GHQ-12), which is a self-administered screening tool designed to detect current mental disturbances and disorders. The original 60-item GHQ has produced a number of progeny

including the GHQ-30, GHQ-28 and the GHQ-12. The GHQ-30 and GHQ-12 were based on the questions that provided the best discrimination among the original criterion groups and were designed such that they contained equal numbers of questions where a positive answer showed health or illness (28).

Although the GHQ has been translated into more than 30 languages and validated in adults (297), there has been some caution of its validity in adolescent populations, particularly, in consideration of the rapid developmental and cognitive changes in young people when transitioning from childhood to adolescence as robust data establishing a unitary concept of ‘psychological distress’ across adolescence is not yet available, beyond evidence reviewed in adolescents at the older end of the spectrum (females aged 15–19 and males aged 17–19) in the UK and Hong Kong. (298).

Another debatable aspect of the GHQ has been the number of mental health domains, which the tool is actually measuring. The literature on the psychometric evaluation of the GHQ-12 mostly suggests that the tool is a valid measure of psychiatric morbidity (i.e. It measures what it purports to measure), and also a reliable measure (i.e. measurement error is low). Examination of the factor structure has however repeatedly led to the conclusion that the GHQ-12 measures psychiatric morbidity in more than one domain (299). Several proponents of this school of thought appeared to be having consensus that the GHQ-12 measured psychiatric dysfunction in three domains, social dysfunction, anxiety and loss of confidence (300).

However, more recent evidence has suggested that conventional psychometric assessments using factor analysis had led to the erroneous conclusion that the GHQ-12 is multidimensional, ignoring the possibility that this was an artefact of the analysis. Structural equation modelling of the GHQ-12 data of the 2004 cohort of the Health Survey for England provided convincing data that GHQ-12 is best thought of as a one-dimensional measure with response bias. That is to say, the GHQ-12 appeared to measure a single dimension, but with greater error on the negatively phrased items (301).

The GHQ-12 was used in the National Health Survey 2010 as part of a larger structured survey questionnaire; to measure mental health during the face-to-face interviews with Singapore residents aged 18 to 69. Cut-offs for poor mental health (score larger than 3) were based on an earlier validation MOH study conducted in 2003 (21).

De-identified data identifying NHS 2010 respondents as “normal” or “poor” mental health status were provided for this analysis.

### **7.3.3 Growth trajectory variable**

Changes in adiposity over time can be based on the change in BMI, or the proportional (percentage) change in BMI, or the change in BMI Z-score or centile (168). BMI was available in 10 physical examinations (from age 7 to 16) based on physical measurements of height and weight of students by a physical education teacher using standard weighing and height machines. These anthropometric data were recorded and submitted to the Ministry of Education (MOE) as part of the on-going monitoring of physical fitness and health screening under the Trim and Fit

(TAF) Program. Trained nurses measured another set of physical measurements of height and weight of students during the Health Promotion Board (HPB) annual school health screening visits. Data from these visits were recorded and submitted to HPB. Data linkages between TAF and SHS were constituted to establish the SLLCC so as to obtain repeated measurements of height and weight regardless of the setting in which the physical examinations were made. Details of the data preparation process were described in Chapter Three.

For the purposes of this study, sex-specific BMI-for-age Z-scores were standardised for all students in the study cohort using the new Stata command “zanthro” (172). Briefly, this extension converted child anthropometric data to Z-scores using the LMS method and the reference data available from the 2000 CDC Growth Reference, the British 1990 Growth Reference, the WHO Child Growth Standards, the WHO Reference 2007, the UK-WHO Preterm Growth Reference, and the UK-WHO Term Growth Reference. In the SLLCC, standardised BMI-for-age Z-scores were derived from WHO child growth standards so that results can be internationally more comparable.

### **7.3.4 Covariates**

#### ***7.3.4.1 Gender, race and smoking status***

Gender and race information were available for all students in the study cohort and were considered as potential risk factors for influencing obesity and poor mental health. Gender and race had been reported to have significant early life influences for class membership in studies that identified developmental trajectories of overweight in children and adolescents (173). A cross-sectional study investigating BMI of Chinese, Malays and Indians in Singapore has

consistently showed that for males there were little ethnic differences, however, for females, Malays and Indians were significantly more obese than Chinese (156), consistent with the National Health Survey 2010 findings (21). Findings from the Singapore Cardiovascular Cohort Study (156) reported that Indians had a threefold increased relative risk of incident CHD (RR=3.1, CI: 2.0–4.8) compared with Chinese and Malays, after adjusting for age, ethnic group and other risk factors (LDL-Cholesterol, HDL-Cholesterol, Triglycerides, BMI, smoking, diabetes, hypertension and alcohol use).

The status of being “a daily smoker” as surveyed in the NHS 2010 was included as a potential risk factor for obesity and mental health wellbeing. “A daily smoker” is defined in the NHS2010 as someone who “smokes cigarettes at least once a day (including people who smoke every day but have to stop temporarily because of religious fasting or medical reasons)” (21). Findings from NHS2010 reported that the crude prevalence of daily smoking among Singapore residents aged 18 to 69 years was 21.8% in males and 3.5% in females. Smoking rate was highest in Malays (18.6%) followed by Indians (12.1%) and Chinese (11.7%). Of relevance to this study was the observation that the mean age at which young smokers aged 18 to 24 years established their smoking habit was 17 years. Male daily smokers aged 18 to 24 years first tried smoking at the mean age of 14 years while female daily smokers in the same age group first experimented with smoking at the mean age of 15 years. Also, the prevalence of smoking in young male adults declined significantly from 25.5% in 1998 to 13.4% in 2004 ( $p<0.05$ ). Among young female adults, smoking prevalence remained about the same, 5.9% in 1998 and 5.8% in 2004 (21).

#### ***7.3.4.2 Age at onset and duration of obesity***

Here we adapt the methodology of defining the age and duration of a weight status (obesity, overweight or underweight) in the Abdullah paper (51). “The beginning of an individual’s obesity interval was defined as the first examination of their period of two consecutive occurrences of obesity and the individual was considered to be continuously obese until the first of two consecutive non-obese examinations. Defining the onset of obesity as two consecutive obesity measurements (correlating with approximately 2 years of being continuously obese) accommodated potential misclassification of body weight, particularly between the upper borderline of the ‘overweight’ BMI category and the lower borderline of the ‘obesity’ category”. The same method is applied to define age at onset and duration of overweight and underweight (51).

#### **7.3.5 Statistical analysis**

Latent class growth mixture models (LCGMM) were first employed to characterise latent BMI-for-age Z-score trajectories in the study population (258). LCGMM is a semi-parametric statistical technique used to analyse longitudinal data. It is used when the data follows a pattern of change in which both the strength and the direction of the relationship between the independent and dependent variables differ across cases (258). LCGMMs were fitted to characterise the optimal number of latent trajectories of BMI-for-age Z-scores over time from age 7 to 16. Models with two to five classes were estimated, beginning with the simplest model. Model fit for each of the 5 models was evaluated, in part, using the Bayesian Information



Criterion (BIC) (259). Successive comparisons of the BIC were made beginning with the 2-class model, with lower values suggesting better model fit. The final selection of the optimal number of latent classes would be dependent on the point in which the BIC values start to level off. Finally, the models were visually inspected for their theoretical and practical coherence with a preference for simpler and more parsimonious models (259).

To ascertain whether the later health outcomes varied by BMI Z-score trajectory during childhood and adolescence, class membership for each subject was used as a predictor (covariate) on their mental health well-being status in 2010. The main dependent variable was GHQ12 score indicating mental wellbeing. The main independent explanatory variables added to the logistic regression model were latent trajectory class, age at onset and duration of obesity, overweight and underweight, median BMI Z-score from age 7 to 16, smoking status in 2010, gender and race.

Four models were estimated using multivariate logistic regression. Model 1 included latent trajectory class membership as a dependent variable only; model 2 controlled for gender; model 3 controlled for gender plus three anthropometric measures, namely, duration of obesity, age at onset of overweight and underweight; model 4 included all variables and was considered as the fully-adjusted model. For all models, the probability of obtaining the chi-square statistic given that the null hypothesis of no effect is true was obtained, together with BIC values. Statistical significance is defined as p-value less than 0.05. The study assumed that unobserved heterogeneity is the same across the compared latent growth trajectory classes or groups (302).

Lastly, data missingness was handled using full information maximum likelihood under the assumption of missing at random. Mplus software version 6.12 was utilised to conduct the LCGMM analyses (148) and Stata 12.0 (149) was used to conduct multivariate analyses to compute means, standard deviations and percentages and logistic regression analyses to assess odds ratios (OR) and 95% confidence intervals (CI).

Singapore Medical Dental Board gave ethical approval for the study.

## **7.4 Results**

A total of 519 out of 598 students (86.8%), aged 18 to 26 from the NHS 2010 were successfully matched with the SLLCC data sets. This allowed retrospective data linkage of up to 10 repeated BMI measurements of the subjects when they were in schools from age 7 to 16 to their later life health outcomes in 2010. Specifically, this study used differential membership of latent BMI Z-score trajectory classes during childhood and adolescence as one of the main determinants to mental health well-being (measured by GHS12 score).

Table 55 shows the socio-demographic profile of this study cohort, the NHS2010 survey respondents and the Singapore resident population aged 18 to 79 years. Table 56 provides a more detailed breakdown of gender within each of the five race groups used for the analysis. Table 57 shows the age-specific prevalence (%) of poor mental health by gender reported in the NHS 2010. Findings from NHS2010 reported that the prevalence of poor mental health was highest in the age group 18 to 29, with 14.1% in males and 22.6% in females.

**Table 55 Socio-demographic profiles of SLLCC/NHS2010 linked study sample, the National Health Survey 2010 and the Singapore resident population aged 18 to 79 in 2010**

Characteristics	Study sample (n=519)	NHS2010 <sup>a</sup> (n=4,337)	Resident population (Census 2010, n=3,771,000)
<b>Gender</b>			
Males	47.6	48.4	49.2
Females	52.4	51.6	50.8
<b>Age (years)</b>			
18 – 29	100	18.2	21.6
30 – 39	0	22.8	21.4
40 – 49	0	25.2	21.9
50 – 59	0	18.4	19.1
60 – 69	0	8.5	10.5
70 – 79	0	6.9	5.5
<b>Ethnic Group</b>			
Chinese	31.2	31.2	75.6
Malay	31.2	29.9	12.3
Indian	26.8	31.2	8.8
Others	10.8	7.8	3.2

Notes:

<sup>a</sup> - The National Health Survey (NHS) is part of the Ministry of Health's on-going surveillance of the health status of Singapore. The NHS 2010 was the fourth in a series of surveys conducted once every six years to assess and monitor the health of the Singapore population.

**Table 56 Gender and race distribution in the SLLCC/NHS2010 linked study sample of 519 individuals**

NHS2010 study sample (Aged 18 to 26)		
Race group	Male (%)	Female (%)
Chinese	76 (30.8)	86 (31.6)
Malay	76 (30.8)	86 (31.6)
Eurasian	0 (0.0)	2 (0.7)
Indonesian	21 (8.5)	27 (9.9)
Indian	69 (27.9)	70 (25.7)
Others	5 (2.0)	1 (0.4)
Total	247 (47.6)	272 (52.4)

**Table 57 Age-specific prevalence of poor mental health by gender in the National Health Survey 2010**

Age (years)	Males	Females	Total
18-29	14.1	22.6	18.4
30-39	13.9	18.4	16.2
40-49	14.6	10.9	12.7
50-59	5.3	7.8	6.5
60-69	6.8	6.3	6.6
18 - 69	11.5	14.1	12.9

**Table 58 Summary statistics for BMI Z-scores in SLLCC/NHS2010 linked study sample of 519 individuals**

BMI Z-score at age	No. Of records	Median	Mean	Std. Dev.	1st Quartile	3rd Quartile	Skewness	Kurtosis	% Missing
7	242	-0.44	-0.27	1.37	-1.12	0.46	0.64	3.33	53.37
8	220	-0.32	-0.16	1.47	-1.18	0.78	0.26	2.91	57.61
9	232	0.04	0.08	1.51	-1.07	1.23	0.08	2.22	55.3
10	266	0.16	0.09	1.58	-1.1	1.32	-0.08	2.30	48.75
11	315	-0.04	0.02	1.44	-0.92	1.17	0.01	2.42	39.31
12	368	0.76	0.74	1.79	-0.65	2.16	-0.05	2.33	29.09
13	351	0.28	0.52	1.71	-0.85	1.74	0.22	2.17	32.37
14	423	-0.01	0.36	1.71	-0.87	1.61	0.35	2.41	18.5
15	439	0.07	0.34	1.68	-0.83	1.39	0.43	2.57	15.41
16	379	-0.09	0.05	1.46	-0.99	0.87	0.49	2.92	26.97
<b>Total n</b>	3,235								

Notes:

SLLCC consists of an extensive individual-level dataset of repeatedly measured anthropometric data, from about 2.7 million students born between 1973 to 2003, collected through routine annual school-based health screening in Singapore from 1990 to 2011.

<sup>a</sup> –Skewness measures the degree and direction of asymmetry. A symmetric distribution such as a normal distribution has a skewness of 0

<sup>b</sup> – Kurtosis is a measure of the heaviness of the tails of a distribution. A normal distribution has a kurtosis of 3

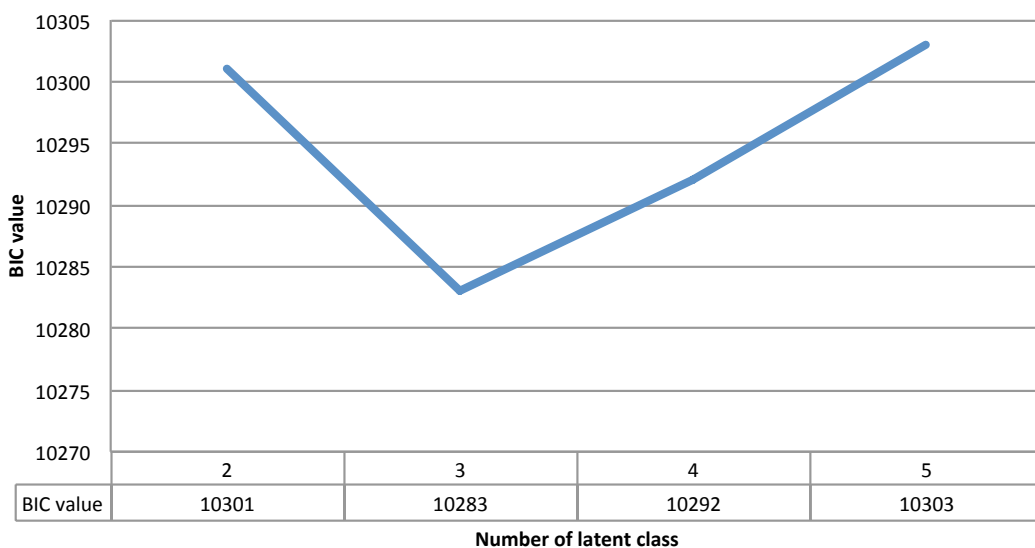
Table 58 describes summary statistics for BMI Z-scores in this study cohort with median Z-score of 0.04, which indicated that most students were at normal weight from age 7 to 16. The mean percentage missingness of the BMI Z-scores was 37.7% across all ages. Average kurtosis

value of 2.56 suggested slightly light-tailed distribution of Z-scores at all ages with a symmetric spread (mean skewness = 0.24). In our study, 96.3% of the cohort had at least 4 annual measurements of their weight and height with 15% having 9 out of 10 maximum measurements in the ten years of childhood and adolescence period (Table 59).

**Table 59 Frequency of BMI measurements by gender in the linked SLLCC/NHS2010 study sample of 519 individuals**

Frequency of number of BMI measurements (from age 7 to 16)										
Gender	1 time	2 times	3 times	4 times	5 times	6 times	7 times	8 times	9 times	10 times
Male (n)	1	1	6	5	71	94	3	29	36	1
Female (n)	1	3	7	8	72	111	2	25	42	1
Total (n)	2	4	13	13	143	205	5	54	78	2
% Of total	0.4%	0.8%	2.5%	2.5%	27.6%	39.5%	1.0%	10.4%	15.0%	0.4%

Model fit indices of the five fitted latent class growth mixture most parsimonious models (LCGMM) suggested that there were three distinct latent trajectory groups (or classes), given that BIC values started to increase in the four and five class models (Figure 43 and Figure 44). Furthermore, the three latent growth trajectories were interpretable in context of the conventional BMI categories of underweight, normal weight, overweight and obese in accordance to WHO BMI-for-age Z-score cut-offs. Average posterior probability of group membership for each of the three trajectory groups were from 0.82 to 0.88 (Table 60). The characteristics of the three-class trajectories model are presented in Table 61.

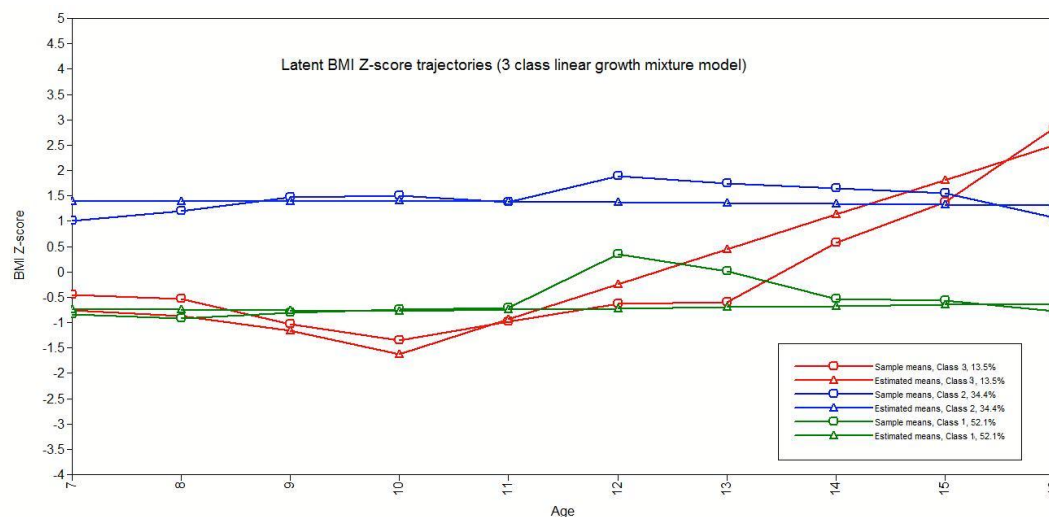


Notes:

BIC = Bayesian Information Criterion; lower values suggest better model fit

The 3-class model was chosen as the final version of the trajectory model, and the corresponding classes were utilized in all subsequent analyses.

**Figure 43 Indicators of model fit (BIC values) in the latent class growth mixture models of the SLLCC/NHS2010 linked study sample of 519 individuals**



**Figure 44 Latent BMI Z-score trajectory groups in the best fitted 3-class trajectories model of the SLLCC/NHS2010 linked study sample of 519 individuals**

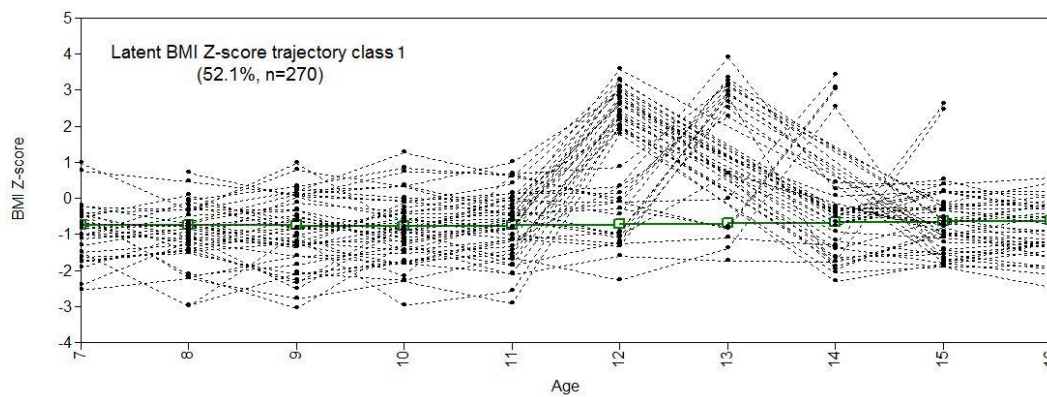
**Table 60 Average latent class probabilities for the most likely class membership (row) by latent class (column) in the best fitted 3-class trajectories latent class growth mixture model of the SLLCC/NHS2010 linked study sample of 519 individuals**

	<b>Class 1</b>	<b>Class 2</b>	<b>Class 3</b>
<b>1</b>	<b>0.816</b>	0.046	0.138
<b>2</b>	0.021	<b>0.861</b>	0.118
<b>3</b>	0.025	0.096	<b>0.879</b>

**Table 61 Characteristics of the latent BMI Z-score trajectory groups in the best fitted 3-class trajectories model of the SLLCC/NHS2010 linked study sample of 519 individuals**

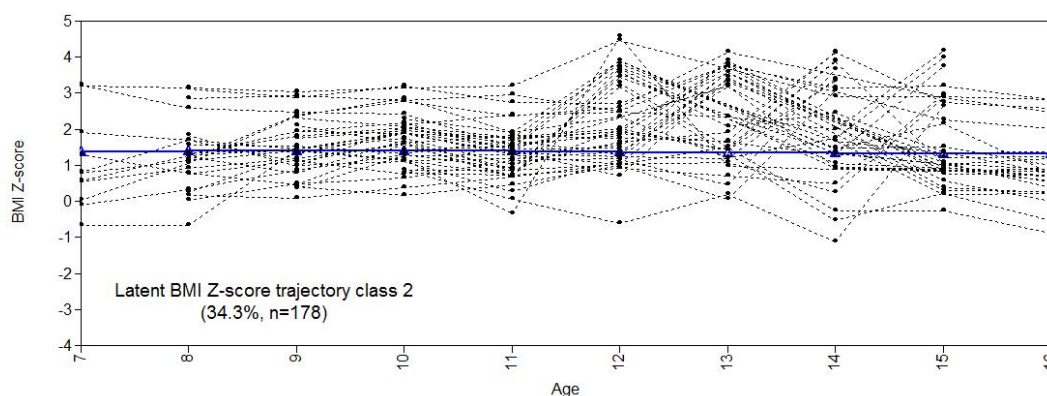
<b>Latent BMI Z-score Trajectory Class</b>			
<b>Characteristics</b>	<b>Consistently Underweight (CUW)</b>	<b>Consistently Overweight (COW)</b>	<b>Adolescence-Onset Obese (AOO)</b>
<b>N (%)</b>	270 (52.1)	178 (34.4)	70 (13.5)
<b>Intercept (S.E)</b>	-0.773 (0.100)	1.405 (0.114)	-1.619 (0.200)
<b>Slope (S.E)</b>	0.024 (0.017)	-0.016 (0.025)	0.686 (0.064)
<b>Race (n)</b>			
Chinese	93	49	20
Malay	82	63	17
Eurasian	0	1	1
Indonesian	19	18	11
Indian	76	40	23
Others	3	2	1
<b>Gender (n)</b>			
Male	120	91	36
Female	153	82	37
<b>GHQ-12 score</b>			
Normal	202	132	53
Poor	51	25	18
<b>Age in 2010 (n)</b>			
18	41	24	0
19	29	25	0
20	17	30	21
21	9	26	26
22	25	13	15
23	28	15	9
24	41	15	2
25	43	14	0
26	40	11	0
<b>Total (n)</b>	<b>273</b>	<b>173</b>	<b>73</b>

The largest “Consistently Underweight” (CUW) trajectory group (n=270, 52.1%) was defined by an average flat trajectory across all ages within the underweight range (BMI: 16 to <18.5 kg/m<sup>2</sup>) (Figure 45). The “Consistently Overweight” (COW) trajectory group (n=178, 34.4%) was characterised by an average trajectory that remained in the overweight range (BMI: 25 to <30 kg/m<sup>2</sup>) through ages 7 to 16 (Figure 46). The “Adolescence-Onset Obese” (AOO) trajectory group (n=70, 13.5%) was characterised by a steadily increasing BMI from being normal weight (BMI: 18.5 to <25 kg/m<sup>2</sup>) at age 10 to becoming obese (BMI: >30 kg/m<sup>2</sup>) by age 16 (Figure 47).

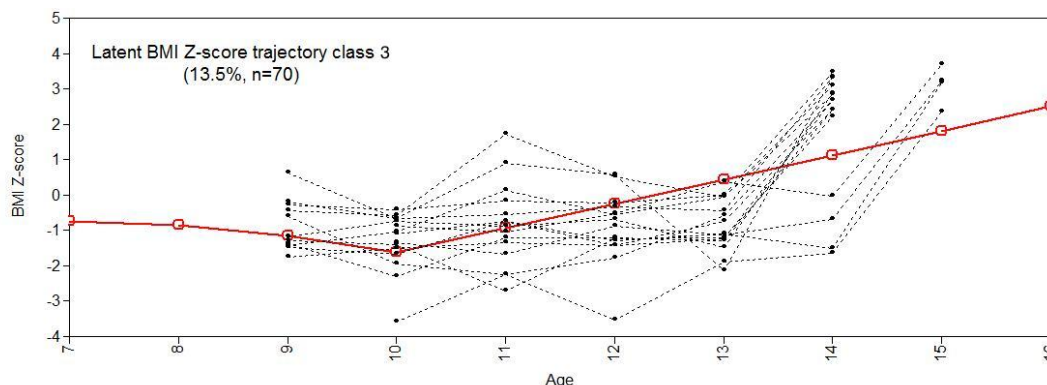


**Figure 45 Random subset of students in the "Consistently Underweight" trajectory group (class 1) in the best fitted 3-class latent class growth mixture model in the SLLCC/NHS2010 linked study sample of 519 individuals**





**Figure 46** Random subset of students in the "Consistently Overweight" trajectory group (class 2) in the best fitted 3-class latent class growth mixture model in the SLLCC/NHS2010 linked study sample of 519 individuals



**Figure 47** Random subset of students in the "Adolescence-Onset Obesity" trajectory group (class 3) in the best fitted 3-class latent class growth mixture model in the SLLCC/NHS2010 linked study sample of 519 individuals

After each individual was assigned exclusively to the trajectory group for which he/she had the highest posterior probability of membership, observed differences between students in the three trajectory classes were first evaluated with Pearson chi-square tests. Significant differences were detected on their age in 2010, age at onset and duration of obesity, overweight and underweight ( $p < 0.001$ ) and non-significant differences were found in the incidence of poor mental health -highest (34%) in the AOO trajectory group as compared to 20% in the COW and

25% in the CUW groups ( $p=0.235$ ), gender distribution ( $p=0.195$ ), race groups ( $p=0.184$ , median BMI Z-score ( $p=0.390$ ) and smoking status in 2010 ( $p=0.221$ ).

Results for the four logistic regression models are presented in Table 62. Findings suggest that when all other variables are held equal, the odds of attaining poor mental health status, versus having normal mental health well-being, were 35% greater if students had a “adolescent-onset obese” trajectory as compared to being “consistently underweight” (Model 1). This effect was strengthened when gender was controlled (OR=1.41, CI: 0.76–2.64) in Model 2.

When further controlling for anthropometric metrics in Model 3, the risks conferred to being in the “adolescent-onset obese” trajectory was slightly attenuated (OR=1.37, CI: 0.73–2.58). At the same time, being “consistently overweight” still had a protective effect (OR=0.32, CI: 0.13–0.78). Mean predicted probabilities are 0.23 for the CUW trajectory (class 1) and 0.09 for the COW trajectory (class 1) and 0.29 for the AOO trajectory (class 3), holding rest of variables at their means (Table 63).

Females were found to be more likely ( $p<0.001$ ) to have a poor mental health well-being (OR=2.17, CI: 1.33–3.52). In terms of anthropometric factors, an increase in duration of obesity by one year was found to increase the odds of poor mental health by 25% (OR=1.25, CI: 1.04–1.50) at  $p=0.02$ . The mean predicted probabilities were 0.18 if the student were never obese between age 7 to 16 and this was observed to increase linearly with every additional year of being obese ( $p<0.05$  for trend). 3% of the cohort was obese for at least two consecutive years (Table 64). Should a student be obese continuously for 10 years, his/her mean odds of poor

mental health could be as high as 60% (Table 65). Figure 48 is a combined plot of the predicted probabilities against duration of obesity by the latent trajectory classes for different levels of the mental health well-being outcome variable.

In the fully adjusted model 4, findings suggest that, when all variables are held constant, age at onset of obesity was not significantly associated with mental health. Minor effects were observed with varying age of onset of overweight and underweight. Being a daily smoker in 2010 also did not influence the odds of a poor mental health status significantly.

**Table 62 Model results of multivariate logistic regression on dependent variable of mental health status (GHQ-12) with reference on "Consistently Underweight" BMI trajectory class and Chinese race in SLLCC/NHS2010 linked study sample of 519 individuals**

	Model 1 <sup>a</sup>				Model 2 <sup>b</sup>				Model 3 <sup>c</sup>				Model 4 <sup>d</sup>			
Independent variables	OR <sup>e</sup>	<i>p</i>	95% CI <sup>f</sup>		OR	<i>p</i>	95% CI		OR	<i>p</i>	95% CI		OR	<i>p</i>	95% CI	
Latent BMI Z-score class																
Consistently Overweight	0.75	0.28	0.44	1.27	0.80	0.40	0.47	1.36	0.32	0.01	0.13	0.78	0.38	0.06	0.14	1.03
Adolescent-Onset Obese	1.35	0.35	0.73	2.49	1.41	0.28	0.76	2.64	1.37	0.33	0.73	2.58	1.40	0.31	0.73	2.68
Other covariates																
Female					2.05	0.00	1.27	3.31	2.17	<0.01	1.33	3.52	2.28	<0.01	1.38	3.78
Duration of obesity									1.25	0.02	1.04	1.50	1.21	0.18	0.92	1.61
Age at onset overweight									1.08	0.08	0.99	1.17	1.11	0.09	0.99	1.25
Age at onset underweight									0.95	0.05	0.90	1.00	0.93	0.15	0.84	1.03
Daily Smoker in 2010													0.67	0.21	0.36	1.25
Median BMI Z-score													0.94	0.72	0.65	1.35
Age at onset obesity													1.02	0.79	0.89	1.16
Duration of overweight													0.88	0.50	0.61	1.28
Duration of underweight													1.05	0.73	0.78	1.42
Race																
Malay													0.78	0.41	0.43	1.42
Eurasian													1.00			
Indonesian													1.20	0.66	0.53	2.73
Indian													0.77	0.40	0.41	1.42
Others													1.00			
Model fit indices																
Probability > chi2	0.24				0.01				<0.01				0.02			
BIC	9.49				6.53				14.57				59.65			

Notes:

<sup>a</sup> Model 1 included latent trajectory class membership as a dependent variable only;

<sup>b</sup> Model 2 controlled for gender;

<sup>c</sup> Model 3 controlled for gender plus three anthropometric measures, namely, duration of obesity, age at onset of overweight and underweight;

<sup>d</sup> Model 4 included all variables and was considered as the fully-adjusted model.

<sup>e</sup> OR = odds ratio;

<sup>f</sup> CI = confidence interval

Statistical significance defined at p-value <0.05

**Table 63 Predictive margins of childhood and adolescence latent BMI Z-score trajectory classes on mental health well being (GHQ-12 score) in the SLLCC/NHS2010 linked study sample of 519 individuals**

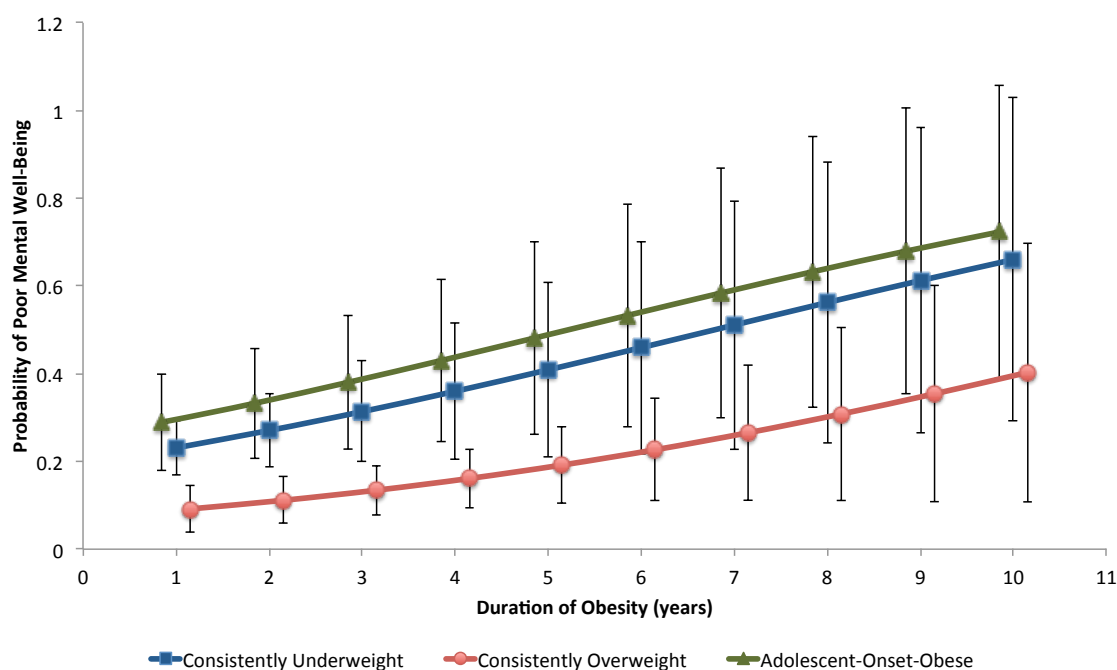
	Margin	Std. Err.	z	P>z	[95% CI]	
Latent trajectory class						
1. Consistently Underweight	0.23	0.03	6.70	<0.01	0.16	0.29
2. Consistently Overweight	0.09	0.03	3.17	<0.01	0.04	0.15
3. Adolescent-Onset Obese	0.29	0.06	4.85	<0.01	0.17	0.41

**Table 64 Number of years being obese (BMI > 30kg/m<sup>2</sup>) by gender in the SLLCC/NHS2010 linked study sample of 519 individuals**

Number of years obese	Gender			
	Male (n)	Female (n)	Total (n)	%
0	217	250	467	90%
2	7	6	13	3%
3	4	2	6	1%
4	8	3	11	2%
5	2	3	5	1%
6	6	3	9	2%
7	2	1	3	1%
8	0	2	2	0%
9	1	2	3	1%
<b>Total</b>	247	272	519	

**Table 65 Predictive margins of duration of obesity (number of years) on mental health well being (GHQ12 score >3) in the SLLCC/NHS2010 linked study sample of 519 individuals**

	Margin	Std. Err.	z	P>z	[95% CI]	
Duration of obesity (years)						
0	0.18	0.02	10.33	<0.01	0.15	0.22
1	0.21	0.02	10.27	<0.01	0.17	0.26
2	0.25	0.03	7.38	<0.01	0.18	0.32
3	0.29	0.05	5.50	<0.01	0.18	0.39
4	0.33	0.07	4.44	<0.01	0.18	0.47
5	0.37	0.10	3.82	<0.01	0.18	0.56
6	0.42	0.12	3.43	<0.01	0.18	0.65
7	0.46	0.14	3.20	<0.01	0.18	0.75
8	0.51	0.17	3.06	<0.01	0.18	0.84
9	0.56	0.19	3.00	<0.01	0.19	0.92
10	0.60	0.20	3.01	<0.01	0.21	1.00



**Figure 48 Predictive margins of latent BMI Z-score trajectory class and duration of obesity on probability of poor mental health status (GHQ-12 score >3) in the SLLCC/NHS2010 study sample of 519 individuals**

## 7.5 Discussion

A pseudo-longitudinal study cohort design was constructed by retrospectively linking individual historical records of childhood and adolescence BMI-for-age Z-scores (ages 7 to 16) with early adulthood (ages 18 to 26) mental health well-being. Implementation of this strategy was feasible in Singapore because of the availability of a unique personal identifier for all Singapore Residents, which permitted data linkage of health outcomes captured in the nationally-representative cross-sectional dataset of NHS 2010 with two large routinely collected repositories of height and weight data recorded through school-based health screening programmes, separately conducted by the Ministry of Education (MOE) and the Health Promotion Board (HPB). The 1990 to 2011 computerised datasets from the MOE and HPB had since been consolidated to form the Singapore Longitudinal and Life Course Cohort (SLLCC) and this study was a demonstration of the potential extensions of SLLCC in pursuing more meaningful research and better understand anthropometric change over time during childhood and adolescence and its later life implications. To the best of my knowledge and review of published literature in the field of obesity and mental health, this approach was the first of its kind to-date. However, the use of routine school health screening data was not novel in itself (303-305).

In this study of 519 youth (aged 18 to 26) in Singapore, results from latent class growth mixture modelling suggested that there were three distinct growth patterns (Figure 44) during their childhood and adolescence in which 52.1% were “consistently underweight”, 34.4% were “consistently overweight” and 13.5% experienced a steady increase of BMI from age 10 to becoming obese by age 16. This finding was similarly reported in several studies revealing

different patterns of weight changes during childhood (72, 261, 296, 306) and is the first step to determining whether certain patterns are associated with certain later life outcomes.

In the logistic regression model 3 that controlled for anthropometric measures (Table 62), individuals who experienced an “adolescent-onset obese” trajectory (Figure 47) between age 7 to 16 had the highest likelihood of reporting a poor mental well-being or were psychological distressed when they entered adulthood in 2010 as compared to those who were consistently underweight (OR=1.37, CI: 0.73–2.58). Interestingly, being consistently overweight was protective (OR=0.32, CI: 0.13–0.78).

It is important to note that because logistic regression coefficients depend both on effect sizes and on the magnitude of unobserved heterogeneity among the latent growth trajectory classes, one cannot straightforwardly interpret and compare coefficients between models as is normally done in linear regression (302). For example, in this study, being continuously obese for longer periods may confer higher risks of mental health well-being, it may also mean that gender is more important in explaining differences in one trajectory group versus the other.

Compared to the only other study in Singapore exploring associations of BMI and mental disorders, the SMHS did not find any association between overweight/obesity and health-related quality of life in the overall sample, after adjusting for covariates (274). There were a couple of important distinctions between that paper and this study. Firstly, weight was self-reported in the SMHS, whereas trained personnel in this study physically measured weight and height. Physical direct measures for assessing height, weight and BMI had been shown in a systematic review to



be less likely to underestimate weight and overestimate height as compared to self-report measures, although the degree of the trend varied for men and women, and between studies (247).

Secondly, the estimation of the association with the health outcome was based on BMI status at a single point in time while this study used the entire BMI developmental trajectory (change over time) from age 7 to 16 as a determinant for psychological distress later in life. In our study, 96.3% of the cohort had at least 4 annual measurements of their height and weight with 15% having 9 out of 10 maximum measurements in the ten years of childhood and adolescence period. A person's weight and height at any one time during his/her lifetime represents a cumulative result of growth until that point, longitudinal growth trajectories allow a more comprehensive study of factors affecting growth at and from different ages. This study revealed that BMI status is not static but rather, changes dynamically over time, consistent with our understanding that adolescent years are characteristic of changes in body composition, physical fitness and decreased insulin sensitivity during puberty (289).

For example in this study, identification of distinct developmental trajectories of obesity separated the consistently overweight from those who exhibited an adolescent-onset obesity pattern. This methodology was comparable with a study on white children aged 9 to 16 years old from the Great Smoky Mountains Study (GSMS), a representative sample of rural youth, who were evaluated annually over an 8-year period for height, weight, psychiatric disorder, and vulnerabilities for psychiatric disorder (72). In that study, four trajectories were detected, including one identifying 7.5% of children who started off in the normal weight range during

childhood but became obese over time (rapidly increasing from age 11 to 16) - almost a replica of the “adolescent-onset obese” trajectory identified in my study. However, adolescent-onset obesity was not associated with increased risk of psychopathology in the GSMS whereas a significant association was found in my study.

Thirdly, the health outcomes were different. The SMHS attempted to measure health-related quality of life whereas GHQ-12 was used to determine current mental well-being of a person by assessing normal ‘healthy’ functioning and the appearance of new, distressing symptoms rather than giving a specific psychiatric diagnosis (28).

**So what biological or explanations might support the observation that rapid increase in adiposity from age 10 to 16 and being consistently underweight was associated with poor mental well-being later in life and why being consistently overweight was protective on the other hand?**

In my study, the mean predicted probability of being “consistently overweight” from age 7 to 16 (BMI: 25 to  $<30 \text{ kg/m}^2$ ) leading to a poor mental status later is 0.09, all other available explanatory variables held constant. This is somewhat consistent with what was presented in the systematic review of the association of obesity on depression among longitudinal studies where the pooled odds of overweight exposure at baseline were only mildly increasing risk of depression follow-up among those subjects younger than 20 years old (OR=1.05, CI: 0.86–1.29) (273). It seemed rather that depression was driving the increase of overweight in a sub-group analysis of the review (OR=1.20, CI: 0.87–1.66). I was not able to explore this direction of the

association given that there was only one measure of mental well-being at the end of the study time span.

My observation of the positive association of an increasing BMI from age 10 is based on the effect of weight change patterns itself rather than the effect of weight status measured in an earlier time point with later mental health as compared to other studies that only employed analysis of weight status or weight change with two (307) or four (308) time point measurements only (273).

Therefore, it was challenging to generalise possible mechanisms behind the increase in adiposity and general psychological distress observed in our study with others (273), although there is widely accepted consensus on the critical role of cortisol, which is regulated by the hypothalamic–pituitary–adrenal axis (HPA)(309), which affects the pathogenesis of obesity and stress. Subjects with obesity display alterations in both the HPA-axis and sleep. Although circulating cortisol levels are often unaltered in obese individuals, the HPA-axis appears to be hyperactive, as there are tissue-specific changes in cortisol concentrations due to differential expression of 11 $\beta$ -hydroxysteroid dehydrogenase Type 1 (an enzyme found in adipose tissue) (309). Thereafter, activity of the HPA axis appears to be altered in both depressed (310) and obese (309) adults and unfortunately less is known about children or adolescents, although a recent review suggested that early stressful life events may provoke alterations of the stress response and thus of the HPA axis, that can endure during adulthood, predisposing individuals to develop psychopathology later in life (311).

It has been shown recently that obesity increases the risk of depression pronouncedly among Americans (273), and it is possible that the association between weight status and mental status may be culturally sensitive and country-specific. In a group of 2,179 healthy Chinese adolescents aged from 11 to 15 years, it was found that more boys than girls believed themselves as underweight, whereas more girls considered themselves as overweight (312). Those perceived themselves as overweight experienced significantly higher levels of psychological distress and would be more susceptible to experiencing unhealthy behaviour than others who perceived themselves as normal or underweight (312). In a systematic review of evidence to understand the barriers to physical activity experienced by adolescents who were overweight or obese, environmental and interpersonal circumstances were found to reinforce negative self-perceptions in overweight and obese adolescents in school or generalised settings at a critical point in their psychosocial development, thus magnifying their psychosocial vulnerability (313).

All of these hypotheses might explain increasing anxiety and depression when adolescents in our study were aware of their rapidly increasing weight or persistent underweight status. The youth perception of obesity thus needs to be further explored in the socio-cultural diversified multi-ethnic context in Singapore.

This study found a “dose-response” association between duration of childhood obesity and psychological distress during adolescents and early adulthood, which, to the best of my knowledge, is the first study to document such observations in an Asian context within a longitudinal study. Earlier age at onset and duration of obesity had already been found to be

significantly associated with an increased risk of developing Type 2 diabetes in adults (51, 314-316).

Findings suggested that after controlling for gender, an increase in duration of obesity by one year was found to increase the odds of poor mental health by 25% (OR=1.25, CI: 1.04–1.50) at  $p=0.02$ . The mean predicted probabilities were 0.18 if the student were never obese between age 7 to 16, and this was observed to increase linearly with every additional year of being obese ( $p<0.05$  for trend) with increased risk conferred to those who belonged to the “adolescent-onset obese” developmental trajectory class.

The biological mechanism underlying the association of duration of obesity and psychological distress is unclear, at least within the limitations of this study as mental health was only measured broadly with GHQ-12 and “poor psychological distress” in itself, might broadly represents a group of mental disorders in our subjects. Although, psychiatric disorders, especially MDD, bipolar disorders, anxiety and schizophrenia, all share common dysregulated biological pathways, including neurotransmitter imbalances; hypothalamus–pituitary–adrenal (HPA) axis disturbances; dysregulated inflammatory pathways; increased oxidative and nitrosative stress and reduced antioxidant defences; neuroprogression resulting in neurodegeneration, apoptosis, reduced neurogenesis and neuronal plasticity; and mitochondrial disturbances (317, 318). In addition to these underlying complex human physiological disorders, parental factors (for example, level of hostility or warmth towards the child) (319) and obesity-related lifestyle factors, particularly, diet, exercise and sleep have been found to mediate the association between obesity and depression (320).

At the time of the study, neither clinical symptoms nor biological indicators of our subjects were available. There was also no further information on other adverse health conditions, parental factors, diet, eating patterns, history of physical activity and sleep duration for comparison between subjects. Future research should explore these potential mediators and confounders in the association of obesity and mental health in Singapore. In addition, when seeking preventive measures and programs to address obesity and psychological distress, it would be necessary to consider the school setting as a powerful enabling environment to promote adolescent socialisation and address barriers to physical activity (313).

In our case of my pseudo-longitudinal study design, only repeated BMI measurements were recorded annually from age 7 to 16 without repeated screening of mental health well being, obtained only when linked to outcomes reported in NHS 2010. Therefore, the reader should also not directly draw conclusions about causal ordering from these findings given the significant bidirectional associations between depression and obesity (273). In addition, the analyses were not able to account for pre-natal and growth in the first 5 to 6 years of life, which had been shown to exert profound effects (321, 322). For example, low weight gain prior to birth was found to be a priming event for adult mental distress. Even after controlling for the effects of gestational age, early life covariates, and adult risk factors, weight for height gain in early childhood acted to mitigate or elevate the likelihood of mental distress only among those born with low weight for gestational age. The effect of early childhood growth depended also on whether the subject was born asymmetrically small on weight alone or symmetrically small on both weight and length. Furthermore, the period of growth associated with altered likelihood of

mental distress in these groups varied (322). Other age-related adiposity associations with mental health include recent evidence among healthy children that faster growth in the pre-natal period and infancy was positively associated with mental health at early school age (321).

Based on my cohort design, the youngest person aged 18 would have at least two years of missing BMI measurement since only data up to age 16 was available. On the other hand, the oldest person in the cohort aged 26 would have at least 10 years of missing BMI measurements since age 16. Nevertheless, given the increasing evidence of “tracking” or the maintenance of obesogenic risk factors including adiposity itself from childhood to adulthood (54-56, 63), there is a high likelihood that adiposity trends from age 18 would be maintained until age 26.

The main strength of my study lay in the longitudinal nature of the datasets and by having repeated height and weight physical measurements from age 7 to 16, one is able to identify latent growth trajectories (unique distinct patterns of sex specific BMI-for-age over time) as a determinant for psychological distress, measured using a widely validated GHQ-12 screening tool. This approach added insights into the association of obesity and mental disorders beyond the impact of atypical BMI-for-age status at a single point in early time. The main limitation was that the study was not able to determine if growth patterns, exhibited through membership in the three latent trajectory classes, was a cause or consequence of psychological distress. And finally, since the study cohort were sub-groups from two nationally representative datasets - NHS 2010 and SLLCC, the study would suffer from limitations within those two datasets, including under-reporting due to stigma associated with mental health problems in Singapore (in the former case)

and high proportion of missingness in such large routinely collected data repositories that were originally not intended for research purposes (in the latter case).

## 7.6 Conclusion

The association of obesity and depression had been well established in both cross-sectional and longitudinal studies (273, 282, 283, 288). However, less is known about the influence of BMI developmental trajectories during childhood and adolescence on mental health well-being in early adulthood. Findings from my study suggested individuals who experienced a distinct developmental trajectory of an increasing rate of weight gain from age 10 resulting in obesity at age 16 was associated with 37% increased risk of attaining a poor mental health well-being at a later time in 2010, all else held constant. This effect affects females more so than males. The study also added insight into the influence of varying age at onset and duration of obesity among Singaporean children and adolescents. Study results appeared to suggest that age at onset of obesity was not significantly associated with mental health and minor effects were observed with varying age of onset of overweight and underweight. However, cumulative duration of obesity during childhood and adolescence would confer significant risks of psychological distress later in life.

In conclusion, a life course approach to improving mental health well-being of Singaporeans must be taken, especially since an increasing childhood obesity burden is likely to be associated with increasing psychological disorders later in life.



## **Chapter 8: Summary of findings and discussion**

### **8.1 Introduction**

The overall aim of this thesis is to characterise anthropometric change among Singapore youth from 1990 to 2011 and explore their latent growth trajectories during childhood and adolescence on later health outcomes. In this final discussion chapter, I summarise the most important and most novel findings from the research and discuss its public health implications, particularly, in Singapore's context. Areas for future work are also proposed as part of my concluding remarks.

### **8.2 Singapore context**

At present only a few countries have in place growth monitoring systems despite recommendations from the World Health Organization (WHO) that national programmes aimed at the prevention of overweight and obesity should include the assessment of all children up to 18 y of age at least once a year and include routine collection of weight and height measurements for the early identification of children at risk of overweight and obesity (323). Before I conducted this research, in Singapore all routinely collected height and weight data from school-based health screening in almost all of 357 primary, secondary and tertiary schools were also reserved for internal growth monitoring of students by the Ministry of Education and Health Promotion Board. It was clear to me that analysis of such routine data could potentially be used to produce reliable indicators of changes in long-term nutritional status (324).

The effect of exposures to unique weight change trajectories during childhood and adolescence on later life health outcomes, rather than focussing on a single BMI at one time period, is at the core of my thesis. As such, I conceived the idea of establishing a new

longitudinal cohort that could provide repeated anthropometric measurements of children and adolescents annually from ages 7 to 16. This would be achieved by record linkage of two large school-based health-screening programmes. Another dataset of relevance to this thesis was the National Health Survey 2010. Summaries of both datasets are described in the next section 8.3.

### **8.3 Summary of the main datasets used in this thesis**

#### **Singapore Longitudinal and Life Course Cohort (SLLCC)**

The Singapore Longitudinal and Life Course Cohort (SLLCC) is a new longitudinal cohort, which I constructed to form the basis of the analyses reported in this thesis. The main strength of the SLLCC is the availability of up to 10 repeated measurements of sex-specific BMI-for-age Z-scores from age 7 to 16 of about 2.7 million students born from 1973 to 2003, collected through routine annual school-based health screening in Singapore from 1990 to 2011. About 1,013,325 (37.4% of total) subjects have at least five repeated physical measurements of their weight and height from age 7 to 16.

The first data source was the School Health Service (SHS) database from Health Promotion Board. This dataset captured information routinely collected from an on-going annual health screening dataset of 95% of all school children at selected academic levels: Primary One and Five/Six and Secondary One, Two and Four. Data were computerised from 1990 to 2011 while paper archives were available for earlier years. Annually, about 44,000 new student records were added since 2000. A trained nurse determined weight and height at respective school health screening visits.

The second data source was the Trim and Fit (TAF) database from the Ministry of Education. This dataset similarly captured information routinely collected from an annual health screening dataset of school children at all academic levels in all primary schools (for ages 6 to 12) and secondary schools (for ages 13 to 16) in Singapore. However, data were computerised from 1997 to 2011 only. In TAF examinations, physical education teachers using calibrated weighing and height measurement machines took height & weight of each student. See Chapter Three for more details on data preparation and Chapter Four for the cohort profile of SLLCC.

### **National Health Survey (NHS) 2010**

The main health data used in these analyses came from the National Health Survey (NHS), which forms part of the Ministry of Health's on-going surveillance of the health status of Singapore. It provides regular information on the prevalence of major non-communicable diseases such as diabetes mellitus and hypertension and related risk factors like obesity and smoking from a representative sample of the resident population. The NHS 2010 was the fourth in a series of surveys conducted once every six years to assess and monitor the health of the Singapore population. Data collection procedures had been previously described elsewhere (147). In 2010, the NHS also captured information on mental health (21). The 12-item General Health Questionnaire (GHQ-12) was used to assess mental health. Cut-off for poor mental health was based an earlier validation study conducted in 2003 (scored >3) (21). De-identified data identifying NHS 2010 respondents as "normal" or "poor" mental health status was provided for this analysis.

## **8.4 Summary of key novel findings**

### **8.4.1 Effect of weight change on later life health outcomes**

Evidence from thirty studies included in my systematic review suggest that, when compared to maintaining a stable weight during adulthood, large weight gains and loss during adolescence to late adulthood life stages, results in marginal to significant increases in risk of first incidence of CHD and all-cause, CVS and CHD mortality in later life, depending on presence of lifestyle and latent morbidity factors (moderate evidence). In addition, large weight fluctuation across multiple time points increases risks of all-cause, CVS and CHD mortality in later life (strong evidence).

### **8.4.2 Secular trends of childhood obesity**

#### **Age-related trends**

In 1997, 11.6% of the children and adolescent aged 6 to 18 on average were classified as overweight (equivalent to BMI 25 to  $<30\text{kg/m}^2$  at 18 years old) using international sex-specific BMI-for-age cut-offs. 4.2% were considered obese (equivalent to BMI  $>30\text{kg/m}^2$  at 18 years old). Overall, 21.3% of the cohort was under-weight (equivalent to BMI  $<18\text{kg/m}^2$  at 18 years old) with those at ages 6-7 and 17-18 being most affected. After 14 years, the prevalence of overweight and obesity were increased to 15.9% and 6.7% respectively in 2011. A higher prevalence of overweight was observed in boys than in girls across all age groups with the highest increase for boys between age 6 to 8 with a steady decline as they grew up (Figure 4). The overweight trend for girls reached its peak at age 11 and tapered gradually to its lowest at age 18. The “% Underweight” trends for both boys and girls from ages 6 to 18 were similar with the highest prevalence of underweight at 32.8% for girls at age 18 and 29.6% for boys at age 6.

### **Period-related trends**

Prevalence of overweight and obesity across all ages increased from 1997 to 2011 (Figure 8). Boys and girls were most likely to be overweight between ages 9 to 12 with lower proportions overweight at age 6 and 18. The percentage of normal weight students did not differ significantly across years. Age-period trends were decreasing over this period for all grades of thinness in chronological order with grade 2 (equivalent to BMI 16 to  $<17\text{kg/m}^2$  at 18 years old) and 3 (equivalent to BMI  $<16\text{kg/m}^2$  at 18 years old) showing greater decline at young ages. Period analysis of % obesity among ethnic youth (ages 6 to 18) showed an increasing trend with average prevalence rates observed for Indonesians and Malays (8.7%), followed by Indians (7.2%), Eurasians (6.8%) and Chinese (4.4%).

### **Cohort-related trends**

Youth born in later cohorts (2003) were observed to have successively higher body weights than earlier-born cohorts (1983, 1988, 1993, 1998), based on the trends observed in cohort-stratified age trends of % obesity and overweight rates (Figure 15). Normal weight prevalence remained relatively unchanged in all cohorts. Cohort trends in all grades of thinness reflected the opposite effect of being successively lower for more recent cohorts than for earlier-born cohorts. Findings suggested that being born during the years 1980 to 1986 had a stronger protective effect on later obesity. This influence varied over the years. Results showed that the percentage obese in 1980 birth cohort was lower when cohort influence was removed. In addition, the cohort effects varied for different ages in the 1998 and 1990 cohorts. Weaker cohort influences were observed for more recent cohort in 1995 and 2000 in general (Figure 21).

### **8.4.3 Possible levelling of obesity trends**

Visual inspection of mean annual (1997-2011) percentage obesity trends among school-age children ages 6 to 18 suggested that in both boys and girls, there might be a possible levelling of the obesity situation after 2006 (Figure 6 and Figure 7). Piecewise linear regression of annual percentage obesity trends in school-age children in Singapore confirmed that there was a plateau in obesity from 2008 to 2011 in both boys and girls (age 13 to 18). This effect was slightly more pronounced for girls than for boys. Between 1997 to 2008, the prevalence of obesity increased linearly in both boys between ages 6 to 12 and girls with the steepest increase seen in boys aged 13 to 18 and in girls.

### **8.4.4 Latent growth trajectories**

The objective of Chapter Six was to characterise latent BMI-for-age z-score trajectories using routine school-based health screening data from 1990 to 2011 (SLLCC) and to determine whether educational transition from primary schools to secondary schools account for shifts in trajectories, and if these patterns differ for boys and girls

For this study, a subset of 1,013,325 subjects from the SLLCC, who had at least five time point measurements of weight and height were included in the analyses. This effective sample size represents the lowest threshold to meet the minimum covariance of 1.00 to run growth mixture models in Mplus.

From 1990 to 2011, results suggested that there were four latent growth trajectories - “Puberty-Only Overweight” (PO), “Normal-Underweight” (NW), “Consistently Obese” (OB) and “Consistently Underweight” (UW) (Figure 29). The only available independent covariates included in the best-fit model were gender and race groups.

The “Pubertal-Only Overweight” (PO) trajectory group (membership: 29.0%) was characterised by a steadily increasing BMI from being normal weight (BMI: 18.5 to  $<25 \text{ kg/m}^2$ ) at age 7 to becoming overweight (BMI: 25 to  $<30 \text{ kg/m}^2$ ) between ages 10 to 13 (corresponding to Tanner stage two/three). Subsequently after puberty, BMI would likely decline to normal weight by age 16. Within the class, almost 40% of the students were overweight and 10% obese by age 10. While the prevalence of overweight declined over time, the prevalence of obesity did not.

The “Normal-Underweight” (NW) trajectory group (membership: 41.2%) was characterised by a trajectory that remained in the normal weight range (BMI: 18.5 to  $<25 \text{ kg/m}^2$ ) through ages 7 to 16. Some members of this group may become underweight or classified as Grade 1 Thinness (BMI: 17 to  $<18.5 \text{ kg/m}^2$ ). In fact, it seemed that about 60% to 70% proportion of the students remained underweight through to age 16.

The “Consistently Obese” (OB) trajectory group (membership: 18.0%) was defined by a (slightly concave downwards) curvilinear average trajectory that started in the obese BMI range at age 7 (BMI:  $>30 \text{ kg/m}^2$ ) and remained obese until age 16. Within-class analysis revealed that 50% of students in this group were already overweight/obese at age 7, increasing to about 75%

by age 8. Prevalence of overweight and obesity continued to plateau, albeit still at high levels, as through primary and secondary schooling, with dips in obesity rates at age 12 and 16.

The “Consistently Underweight” (NW) trajectory group (membership: 11.7%) was defined by an average flat trajectory across all ages. Within this class, about 80 to 85% of students were underweight from the onset.

A key finding of this study that may warrant additional investigation was the identification of the UW trajectory group that comprised 11.7% of the cohort. It should also not be overlooked that about 80% of students in this class were underweight from the onset and remained underweight. At the same time, about 60% to 70% proportion of the students was also underweight in the largest NW trajectory group (41.2% of cohort). Patterns of growth trajectories were also found to differ between males and females, so separate analyses were conducted (Figure 38).

In the PO trajectory group, boys had a steeper increase from age 7 to 10 but girls had a higher initial mean BMI Z-score at age 7. Not many differences were observed for the NW trajectory group. For the OB trajectory group, boys experienced higher fluctuations in BMI than girls, with the latter recording a higher BMI Z-score at age 16. Interestingly, boys ended up being more underweight on average than girls in the UW trajectory group. Within all classes, the mean BMI Z-score for girls were generally lower than boys. There were no significant differences in the heterogeneity of gender and racial group make up between the four trajectories and with the entire cohort.



#### **8.4.5 Growth trajectories and mental health**

In Chapter Seven, a total of 519 out of 598 students (86.8%), aged 18 to 26 from the National Health Survey (NHS) 2010 were matched with the Singapore Longitudinal and Life Course Cohort (SLLCC) data sets so as to link 10 repeated physical measurements of their childhood and adolescence BMI from when they were at age 7 to 16 to their later life mental health well-being (GHQ-12). Older respondents of the NHS 2010 were not included in this study as the oldest birth cohort in the SLLCC that had a complete set of BMI measurements from age 7 to 16 was born in 1984, thus they would be 26 years of age in 2010 (at the time of the NHS).

This study was a demonstration of the potential extensions of SLLCC in pursuing more meaningful research to allow better understanding of the anthropometric change over time during childhood and adolescence and its later life implications. To the best of my knowledge and review of published literature in the field of obesity and mental health, this approach was the first of its kind to-date.

Results from latent class growth mixture modelling in this sample of 519 students suggested that there were three distinct growth patterns (Figure 44) during their childhood and adolescence in which 52.1% were “consistently underweight”, 34.4% were “consistently overweight” and 13.5% experienced a steady increase of BMI from age 10 to becoming obese by age 16. This finding was similarly reported in several studies revealing different patterns of weight changes during childhood (72, 261, 296, 306) and is the first step to determine if certain patterns are associated with certain later life outcomes.

When all other variables are held equal, the odds of attaining poor mental health status, versus having normal mental health well-being, was 35% more likely if students had a “adolescent-onset obese” trajectory as compared to being “consistently underweight” in Model 1. This effect was strengthened when gender was controlled (OR=1.41, CI: 0.76–2.64) in Model 2. When further controlling for anthropometric metrics in Model 3, the risks conferred to being in the “adolescent-onset obese” trajectory was slightly attenuated (OR=1.37, CI: 0.73–2.58). Females were also found to be more likely ( $p<0.001$ ) to have a poor mental health well-being (OR=2.17, CI: 1.33–3.52).

In terms of anthropometric factors, an increase in duration of obesity by one year was found to increase the odds of poor mental health by 25% (OR=1.25, CI: 1.04–1.50) at  $p=0.02$ , when controlled for gender, age at onset overweight and underweight in Model 3. The mean predicted probabilities were 0.18 if the student were never obese between age 7 to 16 and this was observed to increase linearly with every additional year of being obese ( $p<0.05$  for trend). The mean predicted probabilities were 0.18 if the student were never obese between age 7 to 16 and this was observed to increase linearly with every additional year of being obese ( $p<0.05$  for trend). 3% of the cohort was obese for at least two consecutive years. Should a student be obese continuously for 10 years; his/her mean chance of having a poor mental health could be as high as 60%. This risk would increase to 69% if he/she was also in the AOO growth trajectory during childhood (Figure 48).

In the fully adjusted model 4, findings suggest that, when all variables are held constant, age at onset of obesity was not significantly associated with mental health. Minor effects were observed with varying age of onset of overweight and underweight. Being a daily smoker in 2010 also did not influence the odds of a poor mental health status significantly.

## **8.5 Discussion**

The reader may refer to preliminary discussions on these key findings within the respective Chapters of the thesis. Here, I would like to focus the final discussion on the public health implications and methodological considerations for some of the key findings on the underlying dynamics of growth among children and adolescents in Singapore over the past two decades in the context of how these new findings may inform future planning, implementing and impact evaluations of obesity prevention programmes in the country.

### **8.5.1 Effect of weight change on later life health outcomes**

In relation to anthropometric changes during late adolescence and adulthood, the evidence was unclear as previous systematic reviews had been inconclusive in understanding the effects of earlier life weight changes on mortality. Therefore, new findings from my systematic review have key implications for obesity prevention and control programmes as weight fluctuation during mid-life is particularly pertinent in a modern society, like in Singapore, where impromptu dieting and binge eating, can easily lead to weight fluctuations over short periods of time. Thus, it is reasonable to place more emphasis on the importance for adults of maintaining stable weight at a desirable level throughout mid-life and that one should appreciate the impact of weight history in early life on later health outcomes.

The life course approach posits that determinants of adult susceptibility to obesity begin in early childhood and develop over the life course (262) and in any investigation of the long-term effect of weight change (including this thesis) on later life health outcomes, there are features of the human growth trajectory and key developmental milestones, such as the size at birth, adiposity peak (263), adiposity rebound, onset of puberty between 10 and 13 years (264, 265), and anthropometric changes during adolescence and adulthood that are of interest to researchers.

My systematic review complements existing evidence on the established relationships of earlier life developmental milestones on later obesity and other health risk. For example, the evidence is already clear that infants who are at the highest end of the distribution for weight or body mass index or who grow rapidly during infancy are at increased risk of subsequent obesity (328). Other features of the developmental milestones such as size at birth (373), adiposity rebound (374) and adiposity peak (90) (less documented) have also been well examined. Paradoxically, any associations found between early growth may also inherently be less useful considering that adult BMI, in itself, mediates the interaction between early growth patterns and subsequent disease risk (22) and that when change in body size with age is linked to a later adverse outcome, it is the change in size across the whole time interval between the measurements, not just in early life, that is implicated (11).

### **8.5.2 Secular trends of childhood obesity**

Information on secular trends on obesity among children in Singapore is available from a limited number of reliable sources. Before this research, what was known was that the prevalence of obesity has been rising over the years with a rate of 5.33% in 1980 compared to 1.80% in 1976, based on a cross-sectional analysis of 221,988 students in primary one and 218,104 in primary six (249). Obesity was defined as body weight above 120% of Harvard standard weight-for-height in that study (249). When obese Chinese students were stratified by their father's occupation, it was found that significantly greater proportions of children were in the upper and middle social classes compared with the general working population (325). This was one of the first studies that hinted at the association between parent's social economic position and childhood obesity in Singapore.

It is clear that the prevalence of childhood obesity at every age has been increasing from 1997 to 2011 in Singapore (Figure 4), consistent with global reviews of the national prevalence of obesity and overweight among pre-school and school age children in the past five decades in most countries of the world (185), even though Singapore still ranks favourably among countries with the lowest levels of childhood obesity (186).

Generally, researchers often seek to understand secular effects due to differential influence of age, period and cohort on the distribution or development of a health outcomes or disease. Age effects describe the common developmental processes that are associated with particular ages or stages in the life course and represents accumulated exposure or physiological change associated with the process of ageing. Period effects are the results of widespread environmental changes, population-wide exposures that occur at a circumscribed point in time

(184). Notwithstanding the choice of weight classification used, previously published findings were likely to represent mixed secular effects of age, period and cohort (APC) on the magnitude of obesity reported.

However, no statistical model can simultaneously estimate APC effects because of the collinearity among the three variables ( $\text{cohort} = \text{period} - \text{age}$ ) (184). For example, in Figure 8, the graphical representation of age-period effects could be observed as I assumed that there are no cohort effects present in this particular analysis. In which, one can see that the prevalence of overweight and obesity across all ages have been increasing since 1997, however, we have not removed the effects of age in this analysis. In any case, this finding suggests that these trends are likely to be driven by similar increasing population-wide exposures in each corresponding years.

On the other hand, even greater period effects than those observed might have occurred had action not been taken and one cannot overlook the possible mitigating effects of the comprehensive ecological approaches undertaken by HPB to intensify obesity prevention at the individual, family, school, community and national contexts in Singapore. Examples of notable initiatives over the last two decades include the Trim and Fit program in 1992, the National Health Lifestyle Program in 1992, Model School Tuck-Shop Program in 2003, Healthier Dining Program in 2003, Healthier Hawker Centre Program in 2006, “Lose to Win” Program in 2009, Health Ambassadors Program in 2012 and most recently the “1 Million Kg” program which aims to help Singaporeans collectively lose 1 million kilograms over three years in the fight against obesity (92).

Similarly for Figure 15, the assumption that there are no period effects holds as findings suggest that children born earlier in 1983 were less obese than those born in 1988 at the same ages, and the same progressive increase is observed every 5 years later. For this particular analysis on cohort effects, the analysis was extended by adopting the median polish technique that explicitly defines cohort effects as age by period interactions, thereby allowing the non-linear variances to be captured as cohort effects (221-223). The final outputs generated by this strategy allow quantification and removal of cohort effects. As seen in Figure 21, the percentage obese in the 1980 birth cohort was lower when cohort influence was removed.

Interestingly, weaker cohort influences were observed for more recent cohorts in 1995 and 2000 in general. A possible hypothesis might be that there are no differences in the obesity rates among those more recently born, as the exposure to the obesity-promoting environment in Singapore affects all age groups to the same extent. In other words, age and period effects might be asserting a greater effect on obesity rather than effects attributable to being in a different birth cohort. This line of thought is counter to the opinion that being part of a particular birth cohort itself represents an exposure that is rich with explanatory power. The conditions, barriers and resources that each cohort is born into and in which they live their collective lives may uniquely shape the patterns and experiences of health and mortality for that cohort (326).

### **8.5.3 Possible levelling of obesity trends**

This study detected an increase in obesity rates for school-age children aged 6 to 12 and a levelling for those aged 13 to 18 occurring at about the same time around the year 2008. The same growth pattern was observed for boys and girls. This suggested that the environment was

not influencing the age groups in a similar manner although given that the change in trend happened at the same time, strong period effects were likely in effect.

Before commenting on the possible levelling of obesity, it is useful to recall that the changes in adiposity over time in this thesis was measured using BMI Z-score based on the WHO child growth standard reference curves (169), which have been adopted in at least 125 countries. Also, that the WHO standards represent how children should grow, on average, in all countries, when properly fed and cared for, rather than describing how they grew at a particular time and place such as use of the 1994 Singapore growth reference (170).

While our analysis focuses on anthropometric changes from age 7 to 16, the reader should be aware that there are also significant associations of post-natal growth development before age 6 with later body composition (327), which the thesis unfortunately was not able to account for. Generally, in typical childhood growth, BMI increases from birth until 1 y of age reaching an adiposity peak and then decreases until 5–9 years of age. The age at which the BMI begins to increase is the so-called adiposity rebound. Some examples of subtle but important effects include the association of higher later adiposity with both those individuals who have a later adiposity peak and those have an earlier adiposity rebound (251). Also, a systematic review has reported that both large weight at birth and rapid infancy growth after birth is significantly associated with later obesity (328).

There are challenges in pinpointing specific milestones of human growth, as growing up is essentially a continuum of biological developments reflecting changes in body composition at



different ages under varying period and cohort effects in different countries and cultures. Therefore, mathematical methodologies have been postulated to allow an objective and quantitative approach to break down postnatal linear growth into three “distinct” components: namely, infancy, childhood and puberty (329). With this method, researchers were able to more accurately determine the age at onset of childhood phase of growth as 6 to 15 months in Sweden (330). In addition, proponents of the “infancy-childhood-puberty (ICP) growth” model have postulated distinct physiological mechanisms driving body composition change in each period of growing up (329). For example, the infancy component can be deemed as largely nutrition dependent, the childhood component being mostly dependent on growth hormone and the pubertal component largely depending on the synergism between sex steroids and growth hormone (331). Studies in China and Sweden have found that for each month’s delay in the age at onset of the childhood phase of growth, there is a reduction of 0.5 cm in height at 60 month of age (332).

Thus, the thesis findings on secular trends in the obesity prevalence among school-age children in Singapore from age 7 to age 18 during 1997 to 2011 may be subject to the limitation of not having been able to account for confounding from earlier life growth patterns. In any case, for the purposes of this discussion, we assume that childhood begins at age 6 until age 12 and adolescence refers to the period of growth from age 13 to 18.

In a systematic review of 52 studies tracking prevalence of obesity in 17 countries, it was clear that there was a tendency towards a stabilisation of the obesity epidemic in children and adolescents from Australia, Europe, Russia and the USA from about 1999 to 2009 (194). Based

on the findings of my thesis, in Singapore, between 1997 to 2008, the prevalence of obesity increased linearly in both boys between ages 6 to 12 (rate of change at 95% confidence interval was 0.17, CI: 0.12–0.23) and girls (rate=0.11, CI: 0.07–0.15) with the steepest increase seen in boys aged 13 to 18 (rate = 0.28, CI: 0.24–0.32) and in girls (rate=0.15, CI: 0.10–0.20). After 2008, a levelling-off was observed among adolescents while obesity among children continued to climb at an even higher rate (see Chapter Five).

My findings are consistent with strong increases similarly reported in Chinese (333) and Vietnamese (334) children and adolescents. However, it is not clear why Singapore would only observe a levelling off among adolescents only after 2008, almost a decade after similar trends were reported for most of developed countries in the West around 1999. Note that a ‘levelling off’ implies that an increase was followed by stabilisation (194).

Possible explanations are likely to rest on the influence of nutrition factors given that associations between growth and later body composition strongly implicate nutrition as the underlying mechanism (22). The stage of nutrition transition in a country may also explain differences in heterogeneity in body weight by age and gender, and even for the coexistence of both underweight and overweight individuals in a single household (335). Studies that included Chinese populations have shown that, especially in countries experiencing rapid changes in diet and physical activity, a nutrition transition occurs first among urban high-income households and last among rural low-income households (335, 336).

The influence of a nutrition transition has been broadly documented in the Asia region showing marked shifts in the structure of foods and diets consumed (187). There are trends at the national level within Asia and different countries are at different stages of the nutrition transition. In the countries furthest along on the nutritional transition, such as Singapore, with higher fat diets and higher rates of obesity, cancer and cardiovascular diseases together account for close to 60% of deaths. Overall, the nutrition transition in Singapore like other high-income countries in the region begins with a demographic transition away from rural toward a much more urban society; technological change combined with increased urbanisation that leads to a shift from physically active to sedentary occupations; increased use of labour-saving devices at work and home; and changes in income profiles (187).

Whilst evidence from a 2011 systematic review and meta-analysis of the parental and family influence on children's dietary intake suggested weak correlations among US and developed European countries (337), less is known about the relationships in developing countries and societies that are under more remarked social and nutrition transitions, such as in Singapore. More recent studies in Asian populations shed some light on child-parent association in eating habits, albeit still based on small samples. For example, in a study of 922 children aged 5-6 years in Malaysia, mother's nutrition knowledge was found to exert a positive influence on children's eating habits (338). In Hong Kong, 1,779 Chinese mother-child pairs were matched and it was found that maternal knowledge, attitude and self-consumption are positively associated with the child's fruit and vegetable consumption, independent of mother's education level and household income (339).

It must also be recognised that parenting does not occur in isolation. It is embedded within a microsystem (the home) with other physical and economic environmental factors, as well as within broader societal systems (340). For example, the availability of snacks and soft drink vending machines in the adolescents' immediate environment (e.g., schools) could contribute to a higher consumption of unhealthy foods. For example, this may interfere with parental control of children's soft drink consumption at home (340).

Unfortunately, there is limited information regarding the dietary intake of children and adolescences in Singapore to-date. The first and only school health survey in 2006 revealed that, among Secondary 1 to Secondary 4 students (ages 13-16 years old), only 40% and 46% of the students consumed the daily recommended 2 servings of fruit and vegetables daily respectively (225). 29% of them consumed sweetened drinks more than once a day and 52% of them consumed deep fried food more than twice a week (225). Given the limited evidence of the association of parental influences on their offspring's eating habits reported in Asian and Western cultures, it is not clear whether trends in dietary intake of Singapore adults based on findings of the National Nutrition Surveys (NNS) in 1993 (341), 1998 (342), 2004 (343) and 2010 (344) may be useful as a probable proxy of dietary intake of Singapore children and adolescences over the past two decades.

From comparing the 2004 and 2010 NNS findings, there was a significant increase in the mean daily intake of wholegrain products among adult Singapore residents, from 0.19 servings in 2004 to 0.76 servings in 2010. Approximately three in ten adult Singapore residents consumed at least one serving of wholegrain products daily in 2010 (27.0%) compared to 8.4% in 2004.

However the consumption of fruit and vegetables dropped from 1.37 and 1.90 servings to 1.27 and 1.78 servings per day over the past six years, respectively. Fewer Singapore residents met the Guidelines for fruit (25.4% versus 29.0%) and vegetables (31.2% versus 42.2%) in 2010 compared with in 2004. In addition, fewer Singapore residents consumed at least two servings of both fruit and vegetables in 2010 compared with in 2004 (11.2% versus 14.3%) (344).

Breakfast and dinner are the two most likely meals of the day, in which, school-age children eat together with their parents. In Singapore, in 2010, about 55.6% of adult Singapore residents reported usually consuming breakfast at home and most had home-prepared dinner (65.5%) while another 28.3% had dinner at hawker centres. Hawker centres are open-air food centres where several local food stalls are co-located for convenience to residential areas. In contrast, the proportion of Singapore residents who reported eating at home for dinner dropped significantly by 8.1% points compared with 2004 (344).

Therefore, with lesser opportunities for home-cooked food, presumably healthier than eating out in restaurants, it may explain why an increasing obesity trend is still observed for children aged 7 to 12 but it does not fully explain the plateau observed among adolescents aged 13 to 16. Possibly, parental influence on their offspring may diminish as children may be more easily influenced by their peers, marketing of foods and advertisements outside of the home environment. In addition, school-based interventions such as the introduction of the “Trim and Fit Scheme” 10-year program in 1992 and the more recent introduction of Holistic Health Framework (146) by the Ministry of Education in 2008 might have also positively contributed to the levelling off of obesity prevalence among older youth as the focus on managing weight and

fitness levels have been broaden to include the other areas in physical health as well as mental and social health.

As previously cautioned, although a levelling off in the prevalence of obesity is largely supported by the findings of this thesis, it must be kept in mind that the prevalence is higher than ever before and there are reasons to be concerned that the current stable phase in some populations could be followed by increases in the future (194). Given the dearth of information about childhood and adolescent nutrition in Singapore, there is a need to start monitoring dietary intake at home and in schools.

#### **8.5.4 Latent growth trajectories**

Previous studies on growth among Singapore children traditionally reported the prevalence of atypical weight classifications, such as underweight and overweight, in different years without much further information on how children in the entire study grew over the years and whether different groups of students grew differently from each other (210, 211, 249). Until now, the only basis of monitoring the impact of national efforts to reduce obesity was cross-sectional National Health Surveys every 6 years, despite these surveys only collecting data on adults over 18 years old. This approach greatly limited our knowledge about the aetiology of obesity during infancy, childhood and puberty with the magnitude of adult obesity only being detected through the national health surveys.

The importance of understanding the impact of weight history in earlier life on later mortality risk has been clearly demonstrated in the longitudinal cohort of the Helsinki

Businessmen Study, where a group of men with overweight in midlife but normal BMI in old age, in turn, had a significant two-fold increased mortality risk ( $RR=1.9$ ,  $CI: 1.2-3.0$ ) when compared with the constantly normal weight group (111). These findings showed that in old age both normal weight and overweight groups are actually mixtures of groups of men with different weight and cardiovascular risk histories. Of the several existing cohorts in Singapore studying the aetiology of various chronic diseases such as diabetes, cancer, cardiovascular and coronary heart diseases (157, 158, 160), none had explored the possible independent role of early life anthropometric change over time, even though body size and growth cannot be separated conceptually, and demonstrating the influence of growth trajectories on later disease can be complex (345).

While it might be intuitive to assume that the “Normal-Underweight” (NW), “Consistently Obese” (OB) and “Consistently Underweight” (UW) trajectories will likely exist in most populations, it is a novel finding that 29% of students had a “Puberty-Only Overweight” pattern of BMI Z-score change, which is unique and previously unknown in the aetiology of childhood obesity in Singapore (Figure 29).

289,821 boys and girls experienced a “Puberty-Only Overweight” trajectory, which is generally characterised by a steadily increasing BMI from age 7 to becoming overweight between ages 10 to 13. Subsequently after puberty, their BMI declined to normal range by age 16. However, the within class analysis shows that almost 40% of the students were overweight and 10% obese by age 10. While the prevalence of overweight declined over time, the level of obesity did not. It is also useful to note that proportion of those underweight accounted for about

30 to 50% of students as well, which suggests that some of these students may have also experienced being underweight at some point when growing up.

Overall, there are limited studies that investigated long-term health risks of child and adolescent adiposity as an independent effect on later life outcomes in humans (346). Therefore, there is yet no consensus on whether obesity and severe underweight during puberty among adolescence, can be considered as a “sensitive” period, during which an exposure has a stronger effect on development and hence disease risk than it would at other times (52). While some studies suggest that metabolic dysfunction is more severe in adults who became obese during adolescence (347), this assumption was challenged by a 2011 systematic review on childhood obesity and risk of adult metabolic syndrome reported weak associations among 11 studies, except for those who were underweight in childhood but obese during adulthood (348). More recently, animal models also presented evidence that support the notion that peri-pubertal onset of obesity, in fact, does not lead to a more severe metabolic phenotype in the young adult relative to the impact of weight gain after puberty (349).

Given that the pubertal growth spurt affects the amount of fat accumulation and the distribution of fat in different ways in boys and girls (350), it may be that adiposity and puberty may be mutually interacting, thus more research is required to fully determine the possible causal pathways so as to better evaluate the risk of obesity in puberty. Finally, the quality of diet in early life may also be important influencing factors for both childhood adiposity and initiation of menarche. In fact, delays in pubertal timing in response to beneficial dietary habits (higher



intakes of vegetable protein and lower intakes of animal protein) have been postulated to be of substantial public health relevance (351).

### **8.5.5 Growth trajectories and mental health**

In this study sample of 519 youth (aged 18 to 26) in Singapore, results from latent class grown mixture modelling suggested that there were three distinct growth patterns (Figure 44) during their childhood and adolescence in which 52.1% were “consistently underweight”, 34.4% were “consistently overweight” and 13.5% experienced a steady increase of BMI from age 10 to becoming obese by age 16. This finding was similarly reported in several studies revealing different patterns of weight changes during childhood (72, 261, 296, 306) and is the first step to determining whether certain patterns are associated with certain later life outcomes.

In the most fully adjusted logistic regression model, individuals who experienced an “adolescent-onset obese” trajectory between age 7 to 16 had the highest likelihood of reporting a poor mental health or were psychological distressed when they entered adulthood in 2010 as compared to those who were consistently underweight (OR=1.37, CI: 0.73–2.58). Interestingly, being consistently overweight was protective (OR=0.32, CI: 0.13–0.78). Females were found to be more likely ( $p<0.001$ ) to have a poor mental health and well-being (OR=2.17, CI: 1.33–3.52). In terms of anthropometric factors, an increase in duration of obesity by one year was found to increase the odds of poor mental health by 25% (OR=1.25, CI: 1.04–1.50) at  $p=0.02$ . Figure 48 is a combined plot of the predicted probabilities against duration of obesity by the latent trajectory classes for different levels of the mental health outcome variable.

Previous discussions in Chapter 7 compared these findings with those in other countries and settings. Particular attention was drawn to biological mechanisms that might explain why rapid increase in adiposity from age 10 to 16 and being consistently underweight would be associated with poor mental health later in life and why being consistently overweight was protective on the other hand. In this Chapter, I would like to expand the discussion on the implications of these findings in Singapore, especially in the context of existing and possible future youth mental health initiatives.

Currently, there are only two flagship mental health initiatives targeting youths in Singapore. Launched in 2012, the Youth Support Youth Programme offers peer support training while the Bounce Back Stronger Youth Online Kit equips youth with effective coping strategies (352). The Youth Support Youth (YSY) Programme is a customised, holistic mental health training to empower youth between 17-25 years to provide appropriate care and support to peers in their community (353). Upon completion of the three-day workshop, participants graduate to become a “Youth Mental Health Ambassador” and become better versed to provide appropriate support to their peers at schools or community. The “Bounce Back Stronger Youth Online Kit” is part of [breath.sg](http://breath.sg), an existing youth-centric online portal and aims to provide Internet-based resources, including a checklist that provides a general indication of the current range of individual coping strengths and other useful information. A key area that the kit places emphasis on is resilience, which is the capacity to cope with stress, overcome the odds and recover from life’s challenges (353).

There have not been any formal evaluation of the HPB's youth mental health initiatives and in general, studies have found that Internet-based prevention and treatment programs for anxiety and depression in children and adolescents offer more flexibility over traditional face-to-face interventions (354). However, only a limited number of such programs have been adequately evaluated for its effectiveness (354) and unfortunately, there are no studies evaluating initiatives that only provided online self-learning materials, as in the case of Singapore's "Bounce Back Stronger Youth Online Kit".

Given new findings on the negative impact of a rapid rise in adiposity from age 10 to 16 among school-age children with mental health later in life, it will be important for HPB to consider implementation of school-based prevention and early-intervention programmes for depression and anxiety in Singapore, in addition to its existing online outreach platforms.

## **8.6 Areas for future work**

Identification of latent growth trajectories among school-age children and adolescents is a first step to better understand the aetiology of childhood obesity and underweight. My findings suggest that BMI change over time is a dynamic process, which compasses individual- and group-level trends, which may not be easily discerned from traditional analysis of national prevalence across the entire cohort in Singapore.

Therefore, future research in school health screening programs should aim to identify students exhibiting a pubertal-only overweight or consistently obese trajectory, given that obesity during this sensitive period may increase their risk of metabolic complications such as impaired

glucose regulation, hypertension, dyslipidemia, fatty liver disease, and systemic low-grade inflammation (355). Particularly for girls, high adiposity during childhood may lead to early pubertal onset (356), which has been found to be associated with about 15% increased risk associated cardio-metabolic disorders, later adult obesity (357).

In addition to the demonstration study of investigating the association of childhood and adolescent latent growth trajectories on later mental health well-being (Chapter 7), the SLLCC offers cross-disciplinary research between health and other interests. One notable field of interest is the potential association between weight status and children's educational achievement in Singapore. There is already global consensus on the growing rates of childhood obesity and the potential long-term health consequences of obesity have focused public attention on identifying the causes of and solutions to obesity (38, 185, 186). While the health consequences of obesity are potentially serious, obesity may also adversely affect other dimensions of child well being that have long-term and equally important consequences. Specifically, obesity may reduce educational achievement (358-361) and faster weight gain in early infancy, late infancy and early childhood was associated with increased mathematics ratings (321).

Discriminatory behaviour towards overweight and obese children may also bring on depression and cause children to adopt coping mechanisms (e.g., substance use) that could further harm educational achievement (362). One method could be to examine differences in the academic performance of adolescents who exhibit different developmental (BMI) trajectories during their schooling-life. This would be superior to cross-sectional studies because a

longitudinal study design can reveal latent growth patterns over time that may otherwise be overlooked by data collected within a snapshot in time.

Singapore residents worked longer hours in 2005 than five years ago (363). The proportion of resident working persons who worked 60 hours or more per week increased from 17 per cent in 2000 to 19 per cent in 2005. With education and economic opportunities, more mothers are now in the workforce. Of the young and middle-aged couple-based families in the 2005 General Household Survey, between 50 to 60% of them are dual-income nuclear families and are bringing up children without the traditional support structures of grandparents and an extended family of adults (363). While parental employment has many benefits for children's development, notably income, it is also known that when both parents are working, they are more likely to face time constraints, and other challenges to preparing healthy meals (364). As such, it is relevant for national policies and interventions to help improve access to healthy foods in career-focussed society such as Singapore so as to enhance families' eating, physical activity, and sleep patterns, with the aim of improving child weight outcomes (365). From a research perspective, the SLLCC may also offer opportunities to explore relationships between childhood BMI trajectories and parental employment given new evidence that children in dual-earner families, the vast majority of children today, experience greater increases in their measures of BMI compared to their counterparts in single-earner homes.

In the US NICHD's Study of Early Child Care and Youth Development (N = 1107), each additional period both parents were employed is associated with a 3.02 percentile increase in children's BMI, larger than the association with maternal employment alone, and this association

seems consistent across childhood. Further, the number of periods both parents are employed full-time (35 or more hours per week) is also associated with higher child BMI z-scores, but during the preschool period only (366). Understanding these dynamics among Singapore households will strengthen evidence-informed policy development to improve work-life balance and parents' influence on the dietary intake of their children.

### **8.7 Further extension of the SLLCC**

From a methodological perspective, it would be useful to expand on the structure of the SLLCC at the school- and neighbour-level factors as to permit multi-level modelling of the longitudinal BMI Z-scores data sets. For example, consolidating school characteristics such as school autonomy, public/private, and types of curriculum, teacher profile, academic and extra-curriculum performance, neighbourhood walkability index, participation in school health promotion initiatives and other health promotions. While school code was technically available in the original raw data sets from HPB and MOE, it was not meaningful to include them in the analyses because no other information relating to each random code was provided. At the same time, the alpha-numerical nature of the random school code could not be easily merged or manipulated across Microsoft Excel, Access, Stata and Mplus to allow grouping or multi-level hierarchical modelling at both individual and school levels. Naturally, the large number of records complicated data management procedures.

Another area of interest which is not fully explored in this thesis is the influence of the geographical location of each student and school, as in order to support interventions aimed at increasing the level of physical activity at the community or neighbourhood level, it becomes

necessary to have a better understanding of the relationships between social determinants of health, physical activity and where people live. The question is whether characteristics of the built environment in communities influence the extent to which people will engage in physical activity such as walking for utilitarian or for leisure purposes. The Walkability Index or the ‘walkability’ of a community had been conceptualised as the extent to which characteristics of the built environment and land use may or may not be conducive to residents in the area walking for either leisure, exercise or recreation, to access services, or to travel to work (367).

Associations of neighbourhood physical environments with adults and children walking for transport and walking for recreation had been extensively studied (368-371). In the context of my research on anthropometric change among school-age children in Singapore, it would be relevant to explore the relationship between the walkability index of the school or residential home on the level of physical activity of the child or youth.

In the raw data sets of SLLCC, postal code of each student is available though no attempt was made to evaluate its completeness and accuracy. The challenge during the time of data preparation was that there was no efficient method that could geocode up to 2.7 million rows of postal code records in a realistic time frame. If geocoding could be achieved in the SLLCC in the future, it would be possible to assign a Walkability Index to each student’s home, based on GIS systems available at HPB.

Finally, under appropriate controls, de-identified elements of the SLLCC could be made available on the Internet to crowd-source innovative ideas on maximising the potential of these data sets across multiple disciplines, administrative and academic entities and individuals.

Data.gov.sg is the first-stop portal to search and access publicly available data published by the Singapore Government (372). Launched in June 2011, data.gov.sg brings together over 8600 datasets from 60 government ministries and agencies. The next step is to propose that SLLCC datasets be made available on this platform.

## 8.8 Conclusions

This thesis aims to characterise anthropometric change among Singapore youth from 1990 to 2011 and explore relationships of their latent growth trajectories during childhood and adolescence on later health outcomes. The approaches used to estimate age, period and cohort effects are feasible even with routinely collected health screening data. The use of life course epidemiological techniques such as latent growth mixture modelling adds insight into previously unknown growth patterns among school-age children. Findings on the association of differential weight change trajectory across age 7 to 16 on later life psychological distress, albeit for a small study population, could potentially be further explored with future prospective research on mapping the causal pathways linking childhood obesity and mental health. Overall, some of these findings may create new evidence-informed public health imperatives for investments to monitor early childhood growth development so as to mitigate deleterious trends leading to other health, social and economic implications in adulthood.

Establishing a new Singapore Longitudinal and Life Course Cohort (SLLCC) is one of the main legacies of this thesis which I hope will serve as an opportunity to promote collaborative research on the life course in Singapore by offering the largest longitudinal cohort of repeated sex-specific BMI-for-age Z-score measurements of children and adolescents, to-date,



with the potential to link to other existing and future administrative and epidemiological studies at the individual level.

## References

1. Finucane M. National, regional, and global trends in body-mass index since 1980: systematic analysis of health examination surveys and epidemiological studies with 960 country-years and 9·1 million participants. *Lancet*. 2011;377:557-67.
2. Whitlock G, Lewington S, Sherliker P, Clarke R, Emberson J, Halsey J, et al. Body mass index and cause-specific mortality in 900 000 adults: collaborative analyses of 57 prospective studies. *Lancet*. 2009;373:1083-96.
3. McGee D. Body mass index and mortality: a meta-analysis based on person-level data from twenty six observational studies. *American Journal of Epidemiology*. 2005;15:87-97.
4. Flegal K, Carroll M, Ogden C, Curtin L. Prevalence and Trends in Obesity Among US Adults. *JAMA*. 2010;303:235-41.
5. Lissner L, Sohlstro A, Sundblom E, Sjoberg A. Trends in overweight and obesity in Swedish school children 1999-2005: has the epidemic reached a plateau? *Obesity Reviews*. 2010;11:553-9.
6. Ogden C, Carroll D, Curtin L, Lamb MM, Flegal K. Prevalence of High Body Mass Index in US Children and Adolescents. *JAMA*. 2010;303:242-9.
7. Weiss A, Beloosesky Y, Boaz M, Yalov A, Kornowski R, Grossman E. Body mass index is inversely related to mortality in elderly subjects. *J Gen Intern Med*. 2008;23(1):19-24.
8. Barker D. The fetal and infant origins of adult disease. *BMJ*. 1990;301(6761):1111.
9. Paneth N, Susser MW. Early origin of coronary heart disease (the "Barker hypothesis"). *BMJ*. 1995;310(6977):411-2.
10. Henry S, Barzel B, Wood-Bradley R, Burke S, Head G, Armitage J. The developmental origins of obesity-related hypertension. *Clinical and experimental pharmacology & physiology*. 2011.
11. Lucas A, Fewtrell MS, Cole T. Fetal origins of adult disease - the hypothesis revisited. *BMJ*. 1999;319:245-9.
12. Diaz A, Mainous G, Everett C. The association between weight fluctuation and mortality: results from a population-based cohort study. *Journal of Community Health*. 2005;30(3):153-65.
13. Peters E, Seidell J, Menotti A, Aravanis C, Dontas A, Fidanza F, et al. Changes in body weight in relation to mortality in 6441 European middle-aged men: The Seven Countries Study. *International Journal of Obesity*. 1995;19:862-8.
14. Rzehak P, Meisinger C, Woelke G, Brasche S, Strube G, Heinrich J. Weight change, weight cycling and mortality in the ERFORT Male Cohort Study. *Eur J Epidemiol*. 2007;22:665-73.

15. Wannamethee S, Shaper A, Walker M. Weight change, weight fluctuation and mortality. *Arch Intern Med.* 2002;162:2575-80.
16. Nguyen N, Center J, Eisman J, Nguyen T. Bone loss, weight loss and weight fluctuation predict mortality risk in elderly men and women. *Journal of Bone and Mineral Research.* 2007;22(8):1147-54.
17. Lissner L, Odell PM, D'Agostino RB, Stokes J, 3rd, Kreger BE, Belanger AJ, et al. Variability of body weight and health outcomes in the framingham population. *The New England Journal of Medicine.* 1991;324(26):1839-44.
18. Hamm P, Shekelle RB, Stamler J. Large fluctuations in body weight during young adulthood and twenty-five-year risk of coronary death in men. *American Journal of Epidemiology.* 1989;129(2):312-8.
19. Muls E, Kempen K, Vansant G, Saris W. Is weight cycling detrimental to health? a review of the literature in humans. *International Journal of Obesity.* 1995;19(3):S46-50.
20. Jeffery R. Does weight cycling present a health risk. *Am J Clin Nutr.* 1996;63:452S-5S.
21. MOH. National Health Survey 2010. Singapore: Epidemiology & Disease Control Division, Ministry of Health, Singapore, 2010.
22. Wells J, Chomtho S, Fewtrell MS. Programming of body composition by early growth and nutrition. *Proceedings of the Nutrition Society.* 2007;66:423-34.
23. Pickles A. *Epidemiological methods in life course research.* London: Oxford University Press; 2007.
24. Duncan T, Duncan SC, Strycker LA. An introduction to latent variable growth curve modeling. Second ed. Marcoulides G, editor. California 2011.
25. Guyer B, Ma S, Grason H, Frick KD, Perry DF, Sharkey A, et al. Early childhood health promotion and its life course health consequences. *Academic Pediatrics.* 2009;9(3):142-9.
26. Ostbye T, Malhotra R, Landerman LR. Body mass trajectories through adulthood: Results from the National Longitudinal Survey of Youth 1979 cohort (1981-2006). *International Journal of Epidemiology.* 2011;40(1):240-50.
27. Twisk J, Hoekstra T. Classifying developmental trajectories over time should be done with great caution. *Journal of Clinical Epidemiology.* 2012;65:1078-87.
28. Goldberg D, Williams P. A user's guide to the General Health Questionnaire: Windsor: NFER-Nelson; 1988.

29. Kessler R, Aguilar-Gaxiola S, Alonso J, Chatterji S, Lee S, Ormel J, et al. The global burden of mental disorders: An update from the WHO World Mental Health (WMH) Surveys. *Epidemiol Psychiatr Soc.* 2009;18(1):23-33.
30. Chong SA, Abdin E, Vaingankar J, Heng D, Sherbourne C, Yap M, et al. A Population-based Survey of Mental Disorders in Singapore. *Ann Acad Med Singapore.* 2012;41:49-66.
31. Subramaniam M, Abdin E, Picco L, Vaingankar J, Chong SA. Multiple chronic medical conditions: prevalence and risk factors - results from the Singapore Mental Health Study. *Gen Hosp Psychiatry.* 2014;12:S0163-8343.
32. Kessler R, Amminger G, Aguilar-Gaxiola S, Alonso J, Lee S, Ustun T. Age of onset of mental disorders: a review of recent literature. *Curr Opin Psychiatry.* 2007;20(4):359-64.
33. Lee I-m, Paffenbarger RS, Jr. Change in body weight and longevity. *Journal of the American Medical Association.* 1992;268(15):2045-49.
34. Breeze E, Clarke R, Shipley MJ, Marmot MG, Fletcher AE. Cause-specific mortality in old age in relation to body mass index in middle age and in old age: follow-up of the Whitehall cohort of male civil servants. *International Journal of Epidemiology.* 2006;35(1):169-78.
35. Jeffreys M, McCarron P, Gunnell D, McEwen J, Smith GD. Body mass index in early and mid-adulthood, and subsequent mortality: a historical cohort study. *International Journal of Obesity.* 2003;27(11):1391-7.
36. Strandberg TE, Strandberg AY, Salomaa VV, Pitkala KH, Tilvis RS, Sirola J, et al. Explaining the obesity paradox: cardiovascular risk, weight change, and mortality during long-term follow-up in men. *European Heart Journal.* 2009;30(14):1720-7.
37. Corral R et al. Association of body weight with total mortality and with cardiovascular events in coronary artery disease: a systematic review of cohort studies. *Lancet.* 2006;368:666-78.
38. Dietz W. Health consequences of obesity in youth: childhood predictors of adult disease. *Pediatrics.* 1998;101:518-25.
39. Cunningham S, Kramer MR, Narayan K. Incidence of childhood obesity in the United States. *The New England Journal of Medicine.* 2014;370(5):403-11.
40. Parsons TJ, Power C, Logan S, Summerbell CD. Childhood predictors of adult obesity: A systematic review. *International Journal of Obesity.* 1999;23 (SUPPL. 8):S1-S107.
41. Monasta L, Batty D, Cattaneo A, Lutje V, Ronfani L, Lenthe FJv. Early-life determinants of overweight and obesity: a review of systematic reviews. *Obesity Reviews.* 2010;11(10):695-708.

42. Haworth CMA, Carnell S, Meaburn EL, Davis OSP, Plomin R, Wardle J. Increasing heritability of BMI and stronger associations with the FTO gene over childhood. *Obesity*. 2008;16(12):2663-8.
43. Pietilainen KH, Kaprio J, Rasanen M, Rissanen A, Rose RJ. Genetic and environmental influences on the tracking of body size from birth to early adulthood. *Obesity Research*. 2002;10(9):875-84.
44. Hardy R, Wills AK, Wong A, Elks CE, Wareham NJ, Loos RJF, et al. Life course variations in the associations between FTO and MC4R gene variants and body size. *Human Molecular Genetics*. 2010;19(3):545-52.
45. Kaakinen M, Laara E, Pouta A, Hartikainen AL, Laitinen J, Tammelin TH, et al. Life-course analysis of a fat mass and obesity-associated FTO gene variant and body mass index in the Northern Finland Birth Cohort 1966 using structural equation modeling. *American Journal of Epidemiology*. 2010;172(6):653-65.
46. Wardle J, Carnell S, Haworth CM, Plomin R. Evidence for a strong genetic influence on childhood adiposity despite the force of the obesogenic environment. *American Journal of Clinical Nutrition*. 2008;87:398-404.
47. Svensson V, Jacobsson JA, Fredriksson R, Danielsson P, Sobko T, Schioth HB, et al. Associations between severity of obesity in childhood and adolescence, obesity onset and parental BMI: A longitudinal cohort study. *International Journal of Obesity*. 2011;35(1):46-52.
48. Vandenbroeck I, Goossens J, Clemens M. Building the obesity system map: Foresight Tackling Obesity. UK: Foresight, 2007.
49. Gonzalez D, Nazmi A, Victora CG. Childhood poverty and abdominal obesity in adulthood: a systematic review. *Cadernos de Saude Publica*. 2009;25:S427-S40.
50. Abdullah A WR, Stoelwinder JU, de Courten M, Stevenson C, Walls HL, Peeters A. The number of years lived with obesity and the risk of all-cause and cause-specific mortality. *International Journal of Epidemiology*. 2011.
51. Abdullah A, Stoelwinder J, Shortreed S, Wolfe R, Stevenson C, Walls H, et al. The duration of obesity and the risk of type 2 diabetes. *Public Health Nutrition*. 2011;14(1):119-26.
52. Ben-Shlomo Y, Kuh D. A life course approach to chronic disease epidemiology: conceptual models, empirical challenges and interdisciplinary perspectives. *International Journal of Epidemiology*. 2002;31:285-93.
53. Kuh D, Ben-Shlomo Y. A life course approach to chronic disease epidemiology. (Life Course Approach to Adult Health No.2). A life course approach to chronic disease epidemiology. 2004;2(473).

54. Lloyd LJ, Langley-Evans SC, McMullen S. Childhood obesity and adult cardiovascular disease risk: a systematic review. *International Journal of Obesity*. 2010;34(1):18-28.
55. Singh AS, Mulder C, Twisk JWR, Van Mechelen W, Chinapaw MJM. Tracking of childhood overweight into adulthood: A systematic review of the literature. *Obesity Reviews*. 2008;9(5):474-88.
56. Serdula MK, Ivery D, Coates R, Freedman DS, Williamson D, Byers T. Do obese children become obese adults? A review of the literature. *Preventive Medicine*. 1993;22(2):167-77.
57. Hjelmberg JVB, Fagnani C, Silventoinen K, McGue M, Korkeila M, Christensen K, et al. Genetic influences on growth traits of BMI: a longitudinal study of adult twins. *Obesity*. 2008;16(4):847-52.
58. Korkeila M, Kaprio J, Rissanen A, Koskenvuo M. Consistency and change of body mass index and weight. A study of 5967 adult Finnish twin pairs. *International Journal of Obesity*. 1995;19(5):310-7.
59. Twisk J, Kemper H, Mellenbergh G. Mathematical and analytical aspects of tracking. *Epidemiologic Reviews*. 1994;16(2):165-83.
60. Wang Y, Wang X. How do statistical properties influence findings of tracking (maintenance) in epidemiological studies? An example of research in tracking of obesity. *European Journal of Epidemiology*. 2003;18:1037-45.
61. Twisk J. The problem of evaluating the magnitude of tracking coefficients. *European Journal of Epidemiology*. 2003;18:1025-6.
62. Blair S, Shaten J, Brownell K, Collins G, Lissner L. Body weight change, all-cause mortality and cause-specific mortality in the Multiple Risk Factor Intervention Trial. *Annals of Internal Medicine*. 1993;119:749-57.
63. Craigie AM, Lake AA, Kelly S, Adamson AJ, Mathers JC. Tracking of obesity related behaviours from childhood to adulthood: a systematic review. *Maturitas*. 2011;70:266-84.
64. Nakano T, Sei M, Ewis AA, Munakata H, Onishi C, Nakahori Y. Tracking overweight and obesity in Japanese children; a six years longitudinal study. *Journal of Medical Investigation*. 2010;57(1-2):114-23.
65. Biro FM, Huang B, Morrison JA, Horn PS, Daniels SR. Body mass index and waist-to-height changes during teen years in girls are influenced by childhood body mass index. *Journal of Adolescent Health*. 2010;46(3):245-50.
66. Ventura AK, Loken E, Birch LL. Developmental trajectories of girls' BMI across childhood and adolescence. *Obesity*. 2009;17(11):2067-74.

67. Pearl J, Verma T. A theory of inferred causation. *Principles of knowledge representation and reasoning* 1991. p. 441-52.
68. Raudenbush S. Comparing personal trajectories and drawing causal inferences from longitudinal data. *Annual review of psychology*. 2001;52:501-25.
69. Martin R, Velicer W, Fava JL. Latent transition analysis to the stages of change for smoking cessation. *Addict Behav*. 1996;21(1):67-80.
70. O'Brien M, Nader PR, Houts RM, Bradley R, Friedman SL, Belsky J, et al. The ecology of childhood overweight: a 12-year longitudinal analysis. *International Journal of Obesity*. 2007;31(9):1469-78.
71. Nagin D. Analyzing developmental trajectories: a semi-parametric group based approach. *Psychological methods*. 1999;4(2):139-57.
72. Mustillo S, Worthman C, Erkanli A, Keeler G, Angold A, Costello EJ. Obesity and psychiatric disorder: developmental trajectories. *Pediatrics*. 2003;111(4):851-9.
73. Duncan T, Duncan SC. The ABC's of LGM: an introductory guide to latent variable growth curve modeling. *Social and personality psychology compass*. 2009;3(6):979-91.
74. OECD. Obesity update 2012. 2012.
75. Lee J, Heng D, Chia K, Chew S, Tan B, Hughes K. Risk factors and incident coronary heart disease in Chinese, Malay and Asian Indian males: the Singapore cardiovascular cohort study. *International Journal of Epidemiology*. 2001;30(5):983-8.
76. Clarke P, O'Malley PM, Johnston LD, Schulenberg JE. Social disparities in BMI trajectories across adulthood by gender, race/ethnicity and lifetime socio-economic position: 1986-2004. *International Journal of Epidemiology*. 2009;38(2):499-509.
77. Novak M, Ahlgren C, Hammarstrom A. A life-course approach in explaining social inequity in obesity among young adult men and women. *International Journal of Obesity*. 2006;30(1):191-200.
78. Sabanayagam C, Shankar A, Saw SM, Tai ES, Wong TY. The association between socioeconomic status and overweight/obesity in a Malay population in Singapore. *Asia Pacific Journal of Public Health*. 2009;21(4):487-96.
79. Ong SK, Fong CW, Ma S, Lee J, Heng D, Deurenberg-Yap M, et al. Longitudinal study of the socio-demographic determinants of changes in body weight and waist circumference in a multi-ethnic Asian population. *International Journal of Obesity*. 2009;33(11):1299-308.
80. Lee Gan G, Jonathan P. Obesity in Singapore, prevention and control. *Singapore Family Physician*. 2012;38(1):8-13.

81. Toh C, Cutter J, Chew S. School based intervention has reduced obesity in Singapore. *BMJ*. 2002;16(324):7334-427.
82. OHCHR. Study on child's right to health in Singapore. 2012.
83. Williamson D, Pamuk E. The association between weight loss and increased longevity: a review of the evidence. *Annals of Internal Medicine*. 1993;119:731-6.
84. Reubin A, Denis M, John S. Long-term effects of change in body weight on all-cause mortality. *Ann Intern Med*. 1993;119:737-43.
85. Terry D, Susan D. The ABC's of LGM: an introductory guide to latent variable growth curve modelling. *Social and personality psychology compass*. 2009;3(6):979-91.
86. Dietz WH. Periods of risk in childhood for the development of adult obesity--what do we need to learn? *J Nutr*. 1997;127(9):1884S-6S.
87. Kuh D, Ben-Shlomo Y, Lynch J, Hallqvist J, Power C. Life course epidemiology. *Journal of Epidemiology & Community Health*. 2003;57:778-83.
88. Singh-Manoux A, Ferrie J, Chandola T, Marmot M. Socioeconomic trajectories across the life course and health outcomes in midlife: evidence for the accumulation hypothesis? *International Journal of Epidemiology*. 2004;33:1072-79.
89. Niedzwiedz C, Katikireddi S, Pell J, Mitchell R. Life course socio-economic position and quality of life in adulthood: a systematic review of life course models. *BMC Public Health*. 2012;12(628).
90. Silverwood R. Issues in modelling growth data within a life course framework. London: London School of Hygiene and Tropical Medicines; 2008.
91. Erikson E. Identity and the life cycle. New York: International Universities Press; 1959.
92. HPB. Singapore Health Promotion Board 2011 [cited 2013 8th September]. Available from: [www.hpb.gov.sg](http://www.hpb.gov.sg).
93. HPB. The CHERISH Award 2000 [cited 2013 5th May]. Available from: <http://www.hpb.gov.sg/HOPPortal/programmes-article/3128>.
94. WHO. WHO Health Promotion School. Geneva: World Health Organization, 1984.
95. MOE. Journey together towards Holistic Health in Singapore Singapore: MOE; 2011 [cited 2013 9th September]. Available from: [http://www.educatingforhealth.com.sg/index.php?option=com\\_content&view=article&id=62&Itemid=61](http://www.educatingforhealth.com.sg/index.php?option=com_content&view=article&id=62&Itemid=61).



96. Youssef AA, Lohrmann D, Jayawardene W. Use of Data Mining to Reveal Body Mass Index (BMI): Patterns Among Pennsylvania Schoolchildren, Pre-K to Grade 12. *J Sch Health*. 2013;83(2):85-92.
97. Singstats. Education statistics 2010 [cited 2011 14th October]. Available from: [www.singstat.gov.sg/stats/themes/people/edun.html](http://www.singstat.gov.sg/stats/themes/people/edun.html).
98. MOE. Education Statistics Digest. Ministry of Education, 2011.
99. Deurenberg-Yap M, Schmidt G, van Staveren WA, Deurenberg P. The paradox of low body mass index and high body fat percentage among Chinese, Malays and Indians in Singapore. *International Journal of Obesity and related metabolic disorders*. 2000;24(8):1011-7.
100. Deurenberg-Yap M, Chew SK, Lin V, Tan B, van Staveren WA, Deurenberg P. Relationships between indices of obesity and its co-morbidities in multi-ethnic Singapore. *International Journal of Obesity and related metabolic disorders*. 2001;25(10):1554-62.
101. Gallagher D. How useful is body mass index for comparison of body fatness across age, sex and ethnic groups? *American Journal of Epidemiology*. 1996;143:228-39.
102. Lobstein T, Baur L, Uauy D R. Obesity in children and young people: a crisis in public health. *Obesity Reviews*. 2004;5(Supplement 1):4-85.
103. Van Gaal L, Mertens I, De Block C. Mechanisms linking obesity and cardiovascular disease. *Nature*. 2006;444(7121):875-80.
104. Wang Z, Nakayama T. Inflammation, a link between obesity and cardiovascular disease. *Mediators of Inflammation*. 2010;535918.
105. Flegal K, Kit B, Orpana H, Graubard B. Association of All-Cause Mortality with overweight and obesity using standard Body Mass Index categories. *Jama*. 2013;309(1):71-82.
106. Rosengren A, Wedel H, Wilhelmsen L. Body weight and weight gain during adult life in men in relation to coronary heart disease and mortality. *European Heart Journal*. 1999;20:269-77.
107. Dyer AR, Stamler J, Greenland P. Associations of weight change and weight variability with cardiovascular and all-cause mortality in the Chicago Western Electric Company Study. *Am J Epidemiol*. 2000;152(4):324-33.
108. Myers J, Lata K, Chowdhury S, McAuley P, Jain N, Froelicher V. The obesity paradox and weight loss. *The American Journal of Medicine*. 2011;124:924-30.
109. Higgins M, D'Agostino R, Kannel W, Cobb J. Benefits and adverse effects of weight loss: Observations from the Framingham study. *Annals of Internal Medicine*. 1993;119 (7 II):758-63.

110. Sauvaget C, Ramadas K, Thomas G, Vinoda J, Thara S, Sankarnarayanan R. Body mass index, weight change and mortality risk in a prospective study in India. *International Journal of Epidemiology*. 2008;37:990-1004.
111. Strandberg TE, Strandberg AY, Salomaa VV, Pitkala KH, Tilvis RS, Sirola J, et al. Explaining the obesity paradox: cardiovascular risk, weight change, and mortality during long-term follow-up in men dagger. *European Heart Journal*. 2009;30(14):1720-7.
112. Lee D-c, Sui X, Artero E, Lee L-m, Church T, McAuley P, et al. Long-term effects of changes in cardiorespiratory fitness and body mass index on all-cause and cardiovascular disease mortality in men. *Circulation*. 2011;124:2483-90.
113. Harrington M, Gibson S, Cottrell R. A review and meta-analysis of the effect of weight loss on all-cause mortality. *Nutrition Research Reviews*. 2009;22:93-108.
114. Tamayo T, Herder C, Rathmann W. Impact of early psychosocial factors (childhood socioeconomic factors and adversities) on future risk of type 2 diabetes, metabolic disturbances and obesity: a systematic review. *BMC Public Health*. 2010;10(525):(1 September 2010).
115. Ong KK. Early determinants of obesity. *Endocrine development*. 2010;19:53-61.
116. Higgins J. *Cochrane Handbook for Systematic Reviews of Interventions*: The Cochrane Collaboration; 2009. Available from: [www.cochrane-handbook.org](http://www.cochrane-handbook.org).
117. Simon S, Iain DT, Julian PH. Tools for assessing quality and susceptibility to bias in observational studies in epidemiology: a systematic review and annotated bibliography. *International Journal of Epidemiology*. 2007;36:666-76.
118. Thomas B, Ciliska D, Dobbins M, Micucci S. A process for systematically reviewing the literature: providing the research evidence for public health nursing interventions. *Worldviews on evidence-based nursing*. 2004;1(3):176-84.
119. Armijo-Olivo S, Stiles C, Hagen N, Biondo P, Cummings G. Assessment of study quality for systematic review: a comparison of the Cochrane Collaboration Risk of Bias Tool and the Effective Public Health Practice Project Quality Assessment Tool: methodology research. *Journal of Evaluation in Clinical Practice*. 2010.
120. Harris TB, Launer LJ, Madans J. Cohort study of effect of being overweight and change in weight on risk of coronary heart disease in old age. *British Medical Journal*. 1997;314(7096).
121. Stevens V, Jacobs E, Sun J, Patel A, McCullough M, Teras L, et al. Weight cycling and mortality in a large propsective US Study. *American Journal of Epidemiology*. 2012;175(8):785-92.

122. Chei C, Iso H, Yamagishi K, Inoue M, Tsugane S. Body mass index and weight change since 20 years of age and risk of coronary heart disease among Japanese: the Japan Public Health Center-based study. *International Journal of Obesity*. 2008;32:144-51.
123. Chou W-T, Kakizaki M, Tomata Y, Nagai M, Sugawara Y, Kuriyama S, et al. Impact of weight change since age 20 and cardiovascular disease mortality risk: the Ohsaki Cohort Study. *Circulation Journal*. 2013;77:679-86.
124. Willett W, Manson J, Stampfer M, Colditz G, Rosner B, Speizer F, et al. Weight, weight change and coronary heart disease in women. *Journal of the American Medical Association*. 1995;273(6):461-5.
125. Folsom AR, French SA, Zheng W, Baxter J, Jeffery RW. Weight variability and mortality: the Iowa Womean's Health Study. *International Journal of Obesity*. 1996;20:704-9.
126. Samuel P, Neil M, Andrew S. Modeling obesity histories in cohort analyses of helath and mortality. *Epidemiology*. 2013;24(1):158-66.
127. Morris R, Rimm A. Long-term weight fluctuation and non-insulin dependent diabetes mellitus in white women. *Annals of Epidemiology*. 1992;2(5):657-64.
128. Galanis DJ, Harris T, Sharp DS, Petrovitch H. Relative weight, weight change, and risk of coronary heart disease in the Honolulu Heart Program. *Am J Epidemiol*. 1998;147(4):379-86.
129. Rimm EB, Stampfer M, Giovannucci E, Ascherio A, Spiegelman D, Colditz G, et al. Body size and fat distribution as predictors of coronary heart disease among middle-aged and older US men. *American Journal of Epidemiology*. 1995;141(12):1117-27.
130. Walker M, Wannamethee G, Whincup PH. Weight change and risk of heart attack in middle-aged British men. *International Journal of Epidemiology*. 1995.
131. Manson J, Stampfer M, Hennekens CH, Willet WC. Body weight and longevity: a reassessment. *Journal of the American Medical Association*. 1987;257(3):353-8.
132. Boyles A, Harris S, Ronney A, Thayer K. Forest plot view: a new graphing tool. *Epidemiology*. 2011;22(5):746-7.
133. Droyvold W, Nilsen T, Lydersen S, Midthjell K, Nilsson P, Nilsson J, et al. Weight change and mortality: the Nord-Trondelag Health Study. *Journal of Internal Medicine*. 2005;257:338-45.
134. Yarnell J, Patterson C, Thomas H, Sweetnam P. Comparision of weight in middle-age, weight at 18 years and weight change between, in predicting subsequent 14 year mortality and coronary events: Caerphilly Prospective Study. *J Epidemiol Community Health*. 2000;54:344-8.

135. Iribarren C, Sharp D, Burchfiel C, Petrovitch H. Association of weight loss and weight fluctuation with mortality among Japanese American men. *The New England Journal of Medicine*. 1995;333:686-92.
136. NTF. Weight cycling. *Jama*. 1994;272(15):1196-202.
137. Pamuk ER, Williamson DF, Madans J, Serdula MK, Kleinman JC, Byers T. Weight loss and mortality in a national cohort of adults, 1971-1987. *Am J Epidemiol*. 1992;136(6):686-97.
138. De Stavola B, Nitsch D, dos Santos Silva I, McCormack VA, Hardy R, Mann V, et al. Statistical issues in life course epidemiology. *American Journal of Epidemiology*. 2006;163(1):84-6.
139. Cox DR. Regression models and life-tables. *Journal of the Royal Statistical Society Series B-Statistical Methodology*. 1972;34(2):187-220.
140. Singer J, Willett J. *Applied longitudinal data analysis: modeling, change and event occurrence*. Oxford: Oxford University Press; 2003.
141. Gamborg M, Jensen G-B, Sorens T, Andersen P-K. Dynamic Path Analysis in Life-Course Epidemiology. *American Journal of Epidemiology*. 2011;173(10):1131-9.
142. Dulloo A, Jacquet J, Montani J. Pathways from weight fluctuations to metabolic diseases. *International Journal of Obesity*. 2002;26:S46-57.
143. Ventura A, Loken E, Birch L. Developmental trajectories of girls' BMI across childhood and adolescence. *Obesity*. 2009;17:2067-74.
144. Thilagaratnam S. School-based screening for scoliosis: is it cost-effective? *Singapore Med J*. 2007;48(11):1012-7.
145. AsiaOne. HuHF, it's not TAF to be fit. *The Straits Times*. 2008.
146. MOE. Holistic Health Framework Singapore2013 [cited 2013 9th September]. Available from: <http://www.moe.gov.sg/education/programmes/holistic-health-framework/>.
147. Lily C. *National Health Survey 2010*. Singapore: 2010.
148. Muthen BO. *Mplus User's Guide*. Sixth Edition. Los Angeles, CA2011.
149. StataCorp. *Stata Statistical Software: Release 12*. College Station, TX: StataCorp LP; 2011.
150. Schmidt GJ, Walkuski JJ, Stensel DJ. The Singapore Youth Coronary Risk and Physical Activity Study. *Medicine & Science in Sports & Exercise*. 1998;30(1):105-13.

151. Deurenberg-Yap M. Body composition and diet of Chinese, Malays and Indians in Singapore: and their influence on cardiovascular risk factors. *Body composition and diet of Chinese, Malays and Indians in Singapore*. 2000;170.
152. Cheung YB, Machin D, Karlberg J, Khoo KS. A longitudinal study of pediatric body mass index values predicted health in middle age. *Journal of Clinical Epidemiology*. 2004;57(12):1316-22.
153. Lee J, Heng D, Chia KS, Chew SK, Tan BY, Hughes K. Risk factors and incident coronary heart disease in Chinese, Malay and Asian Indian males: The Singapore cardiovascular cohort study. *International Journal of Epidemiology*. 2001;30(5):983-8.
154. Ong S, Fong C, Ma S, Lee J, Heng D, Deurenberg-Yap M, et al. Longitudinal study of the socio-demographic determinants of changes in body weight and waist circumference in a multi-ethnic Asian population. *International Journal of Obesity*. 2009;33:1299-08.
155. Heng D, Lee J, Chew S, Tan B, Hughes K, Chia K. Incidence of ischaemic heart disease and stroke in Chinese, Malays and Indians in Singapore: Singapore Cardiovascular Cohort Study. *Ann Acad Med Singapore*. 2000;29(2):231-6.
156. Lee J, Heng D, Chia KS, Chew SK, Tan B, Hughes K. Risk factors and incident coronary heart disease in Chinese, Malay and Asian Indian males: the Singapore Cardiovascular Cohort Study. *International Journal of Epidemiology*. 2001;30(5):983-8.
157. Lee J, Heng D, Ma S, Chew SK, Hughes K, Tai E. Influence of pre-hypertension on all-cause and cardiovascular mortality: the Singapore Cardiovascular Cohort Study. *International Journal of Cardiology*. 2009;135(3):331-7.
158. Lee J, Ma S, Heng D, Chew SK, Hughes K, Tai E. Hypertension, concurrent cardiovascular risk factors and mortality: the Singapore Cardiovascular Cohort Study. *J Hum Hypertens*. 2008;22(7):468-74.
159. Ei Ei KN, Chin Meng K, E Shyong T, Su Chi L, Subramaniam T, Tien Yin W, et al. Is There a Clear Threshold for Fasting Plasma Glucose That Differentiates Between Those With and Without Neuropathy and Chronic Kidney Disease? The Singapore Prospective Study Program. *American Journal of Epidemiology*. 2009;169(12):1454-62.
160. Narasimhalu K. Study Protocol for the Singapore Consortium for Cohort Studies (SCCS). 2007.
161. Tan J, Ng D, Nurbaya S, Ye S, Lim X, Leong H. Polymorphisms identified through genome-wide association studies and their associations with type 2 diabetes in Chinese, Malays, and Asian-Indians in Singapore. *J Clin Endocrinol Metab*. 2010;95(1):390-7.
162. Saw SM, Shankar A, Tan S, Taylor H, Tan DTM, Stone RA. A cohort study of incident myopia in Singaporean children. *Invest Ophthalmol Vis Sci*. 2006;47(5):1839-44.

163. Soh S, Tint M, Gluckman PD, Godfrey KM, Rifkin-Graboi A, Chan Y, et al. Cohort Profile: Growing Up in Singapore Towards healthy Outcomes (GUSTO) birth cohort study. *Int J Epidemiol*. 2013.
164. Soh S, Lee S, Hoon W, Tan M, Goh A, Lee B, et al. The methodology of the GUSTO cohort study: a novel approach in studying pediatric allergy. *Asia Pac Allergy*. 2012;2(2):144-8.
165. Dubois L, Girard M. Early determinants of overweight at 4.5 years in a population-based longitudinal study. *International Journal of Obesity*. 2006;30(4):610-7.
166. Malhotra R, Malhotra C, Chan A, Ostbye T. Life-Course Socioeconomic Status and Obesity Among Older Singaporean Chinese Men and Women. *Journals of Gerontology*. 2013;68(1):117-27.
167. Jung T, Wickrama K. An Introduction to Latent Class Growth Analysis and Growth Mixture Modeling. *Social and personality psychology compass*. 2008;2(1):302-17.
168. Cole T, Faith M, Pietrobelli A, HEO M. What is the best measure of adiposity change in growing children: BMI, BMI %, BMI z-score or BMI centile? *European Journal of Clinical Nutrition*. 2005;59:419-25.
169. De Onis M, Onyango AW, Borghi E, Garza C, Yang H. Comparison of the World Health Organization (WHO) Child Growth Standards and the National Center for Health Statistics/WHO international growth reference: Implications for child health programmes. *Public Health Nutrition*. 2006;9(7):942-7.
170. De Onis M, Adelheid O, Elaine B, Amani S, Monika B, Chessa L. Worldwide implementation of the WHO Child Growth Standards. *Public Health Nutrition*. 2012;15(9):1603-10.
171. Wang Y, Chen H-J. *Handbook of Anthropometry: Physical Measures of Human Form in Health and Disease*. Baltimore, MD: Springer Science+Business Media; 2012.
172. Vidmar S, Cole T, Pan H. Standardizing anthropometric measures in children and adolescents with functions for egen: Update. *The Stata Journal*. 2013;13(2):366-78.
173. Li C, Goran M, Kaur H, Nollen N, Ahluwalia JS. Developmental trajectories of overweight during childhood: role of early life factors. *Obesity*. 2007;15(3):760-71.
174. Clarke PJ, O'Malley PM, Schulenberg JE, Johnston LD. Midlife health and socioeconomic consequences of persistent overweight across early adulthood: findings from a National Survey of American Adults (1986-2008). *American Journal of Epidemiology*. 2010;172(5):540-8.

175. MOH. Population and vital statistics 2012 [cited 2013 1st November]. Available from: [http://www.moh.gov.sg/content/moh\\_web/home/statistics/Health\\_Facts\\_Singapore/Population\\_And\\_Vital\\_Statistics.html](http://www.moh.gov.sg/content/moh_web/home/statistics/Health_Facts_Singapore/Population_And_Vital_Statistics.html).
176. Nick B, John E, Stephen J. Choosing a longitudinal survey design: the issues. UK: ESRC Research Centre on Micro-social change, University of Essex, 1995.
177. Singstats. Mean years of schooling 2012 [cited 2013 8th December]. Available from: [http://www.singstat.gov.sg/statistics/visualising\\_data/chart/Mean\\_Years\\_Of\\_Schooling.html](http://www.singstat.gov.sg/statistics/visualising_data/chart/Mean_Years_Of_Schooling.html).
178. AGC. National Registration Act (Chapter 201) 2013 [cited 2013 8th December]. Available from: <https://app.agc.gov.sg/>.
179. Virtanen S, Notkola V. Socioeconomic inequalities in cardiovascular mortality and the role of work: a register study of Finnish men. *Int J Epidemiol*. 2002;31(3):614-21.
180. SFI. The Danish National Centre for Social Research: Danish Longitudinal Databases 2013 [cited 2013 8th December]. Available from: <http://www.sfi.dk/english-2631.aspx>.
181. CLOSER. Cohorts and Longitudinal Studies Enhancement Resources 2012 [cited 2014 16th April]. Available from: <http://www.closerprogramme.co.uk/>.
182. Baum C. Stata: The language of choice for time-series analysis? *The Stata Journal*. 2005;5(1):46-63.
183. Nooyens ACJ, Visscher TLS, Verschuren WMM, Schuit AJ, Boshuizen HC, Van Mechelen W, et al. Age, period and cohort effects on body weight and body mass index in adults: The Doetinchem Cohort Study. *Public Health Nutrition*. 2009;12 (6):862-70.
184. Keyes KM, Li G. A multiphase method for estimating cohort effects in age-period contingency table data. *Annals of Epidemiology*. 2010;10:779-85.
185. De Onis M, Blossner M, Borghi E. Global prevalence and trends of overweight and obesity among preschool children. *Am J Clin Nutr*. 2010;92:1257-64.
186. Mercedes dO, Monika B. Prevalence and trends of overweight among preschool children in developing countries. *American Journal of Clinical Nutrition*. 2000;72:1032-9.
187. Popkin B, Horton S, Kim S. The nutritional transition and diet-related chronic diseases in Asia: implications for prevention. Washington, DC: International food policy research institute, 2001.
188. Keats S, Wiggins S. Future diets. UK: Overseas Development Institute, 2014.

189. Chan A. Singapore's Changing Structure and the Policy Implications for Financial Security, Employment, Living Arrangements and Health Care. Singapore: Asia Meta Centre, 2001.
190. Boon W. Child Health in Singapore: past, present and future. *Journal of the Singapore Paediatric Society*. 1979;21(1):22-37.
191. Whitton C, Ma Y, Bastian A, Chan M, Chew L. Fast-food consumers in Singapore: demographic profile, diet quality and weight status. *Public health Nutr*. 2013;2:1-9.
192. HPB. Report of the National Nutrition Survey 2004. Singapore: Health Promotion Board, 2004.
193. Ogden C, Carroll M, Kit B, Flegal K. Prevalence of obesity and trends in body mass index among US children and adolescents, 1999-2010. *JAMA*. 2012;307:483-90.
194. Rokholm B, Baker J, Sorensen T. The levelling off of the obesity epidemic since the year 1999 – a review of evidence and perspectives. *Obesity Reviews*. 2010;11:835-46.
195. Aeberli I, Henschen I, Molinari L, Zimmermann MB. Stabilization of the prevalence of childhood obesity in Switzerland. *Swiss Med Wkly*. 2010;140.
196. Boddy L, Hackett A, Stratton G. Changes in BMI and prevalence of obesity and overweight in children in Liverpool 1998-2006. *Perspect Public Health*. 2009;129:127-31.
197. de Wilde J, Van Dommelen P, Middelkoop B, Verkerk PH. Trends in overweight and obesity prevalence in Dutch, Turkish, Moroccan and Surinamese South Asian children in the Netherlands. *Arch Dis Child*. 2009;94:795-800.
198. Kolle E, Steene-Johannessen J, Holme I, Andersen L, Andersen S. Secular trends in adiposity in Norwegian 9-year-olds from 1999–2000 to 2005. *BMC Public Health*. 2009;9:389.
199. Pearson S, Hansen B, Sorensen T, Baker J. Overweight and obesity trends in Copenhagen schoolchildren from 2002 to 2007. *Acta Paediatr*. 2010.
200. Salanave B, Peneau S, Rolland-Cachera M, Hercberg S, Castetbon K. Stabilization of overweight prevalence in French children between 2000 and 2007. *International Journal of Pediatric Obesity*. 2009;4:66-72.
201. Meigen C, Keller E, Gausche R, Kromeyer-Hauschild K, Bluher S, Kiess W, et al. Secular trends in body mass index in German children and adolescents: a cross-sectional data analysis via CrescNet between 1999 and 2006. *Metabolism*. 2008;57:934-9.
202. Tudor-Locke C, Ainsworth B, Popkin B. Patterns of physical activity and overweight among 7–13-year-old Russian children: a 7-year nationally representative monitoring study. *Res Q Exerc Sport*. 2008;79:10-7.



203. Yoshinaga H, Ichiki T, Tanaka Y, Hazeki D, Horigome H, Takahashi H, et al. Prevalence of childhood obesity from 1978 to 2007 in Japan. *Pediatr Int*. 2009;52:213-7.
204. Dieu H, Dibley M, Sibbritt D, Hanh T. Trends in overweight and obesity in pre-school children in urban areas of Ho Chi Minh City, Vietnam, from 2002 to 2005. *Public Health Nutr*. 2009;12:702-9.
205. Lyu Y, Ouyang F, Ye X, Zhang J, Lee S, Li Z. Trends in overweight and obesity among rural preschool children in southeast China from 1998 to 2005. *Public Health*. 2013;127:1082-9.
206. Olds TS, Tomkinson GR, Ferrar KE, Maher C. Trends in the prevalence of childhood overweight and obesity in Australia between 1985 and 2008. *International Journal of Obesity*. 2010;34:57-66.
207. Benson L, Baer HJ, Kaelber D. Trends in the diagnosis of overweight and obesity in children and adolescents: 1999-2007. *Pediatrics*. 2009;123:e153-8.
208. Ogden C, Carroll M, Flegal K. High body mass index for age among US children and adolescents, 2003–2006. *JAMA*. 2008;299:2401-5.
209. Ogden C, Carroll D, Curtin L, Lamb MM, Flegal K. Prevalence of high body mass index in US children and adolescents, 2007–2008. *JAMA*. 2010;303:242-9.
210. Loke K, Lin J, Mabel D. 3rd College of Paediatrics and Child Health Lecture – The Past, the Present and the Shape of Things to Come. *Ann Acad Med Singapore*. 2008;37(5):429-34.
211. Mabel D, Kwok CL, Lyen K, Lam SL. Secular trend of growth in pre-school children in Singapore. *Asia Pacific Journal of Clinical Nutrition*. 1994;3:61-4.
212. Tan J, Dorajoo R, Seielstad M, Sim X, Ong R-H, Chia KS. FTO variants are associated with obesity in the Chinese and Malay populations in Singapore. *Diabetes*. 2008;57(10):2851-7.
213. Lavanya R, Jeganathan V, Zheng Y, Raju P, Cheung N, Tai E. Methodology of the Singapore Indian Chinese Cohort (SICC) eye study: quantifying ethnic variations in the epidemiology of eye diseases in Asians. *Ophthalmic Epidemiol*. 2009;16(6):325-36.
214. De Onis M, Habicht JP. Anthropometric reference data for international use: recommendations from a World Health Organization Expert Committee. *Am J Clin Nutr*. 1996;64:650-8.
215. WHO. WHO Consultation on Obesity: preventing and managing the global epidemic. Geneva: World Health Organization, 2000.
216. Cole T, Bellizzi M, Flegal K. Establishing a standard definition for child overweight and obesity worldwide: international survey. *BMJ*. 2000;320:1240-3.

217. Lobstein T, Frelut ML. Prevalence of overweight among children in Europe. *Obesity Reviews*. 2003;4:195-200.
218. WHO. WHO Child Growth Standards based on length/height, weight and age. *Acta Paediatr*. 2006(Supp 450):76-85.
219. WHO. WHO child growth standards: growth velocity based on weight, length and head circumference, methods and development. Geneva: World Health Organization, 2009.
220. Sykes P. Errors arising through using the Harvard tables and percentage levels of median weight-for-age in assessing nutritional status. *Archives of Disease in Childhood*. 1977;52:391-4.
221. Tukey J. *Exploratory data analysis*. Reading: Addison-Wesley Publishing Company; 1977.
222. Selvin S. *Statistical analysis of epidemiologic data*. New York: Oxford University Press; 1996.
223. Keyes KM, Utz R, Robinson W, Li G. What is a cohort effect? Comparison of three statistical methods for modeling cohort effects in obesity prevalence in the United States 1971-2006. *Social Science & Medicine*. 2010;70(7):1100-8.
224. Williams A, Henley W, Williams CA, Hurst AJ, Wyatt K. Systematic review and meta-analysis of the association between childhood overweight and obesity and primary school diet and physical activity policies. *International Journal of Behavioral Nutrition and Physical Activity*. 2013;10(101).
225. HPB. *Students' Health Survey 2006*. Singapore: Health Promotion Board, 2006.
226. Kwok CS, Wong ML, Vijaya K, Sandhu NK. Nurturing healthy dietary habits among children and youth in Singapore. *Asia Pac J Clin Nutr*. 2012;21(1):144-50.
227. Lim YP. Sharing Singapore's experience in dietetic practice and school nutrition programmes. *Asia Pac J Clin Nutr*. 2008;17(S1):361-4.
228. Ogden C, Carroll M, Kit B, Flegal K. Prevalence of Obesity and Trends in Body Mass Index Among US Children and Adolescents, 1999-2010. *JAMA*. 2012;307(5):483-90.
229. Olds TS, Tomkinson GR, Ferrar KE, Maher CA. Trends in the prevalence of childhood overweight and obesity in Australia between 1985 and 2008.
230. Ray R, Lim L, Ling S. Obesity in preschool children: an intervention programme in primary health care in Singapore. *Ann Acad Med Singapore*. 1994;23(3):335-41.
231. Yap M, Tan WL. Factors associated with obesity in primary-school children in Singapore. *Asia Pac J Clin Nutr*. 1994;3:65-8.

232. Kurokawa N, Nakai K, Suzuki K, Sakurai K, Shimada M, Kameo S, et al. Trends in growth status among school children in Sendai, Japan, 1994-2003: Leveling-off of mean body height and weight. *Tohoku J Exp Med*. 2008;216:371-5.
233. singhal N, Misra A, Shah P, Rastogi K, Vikram NK. Secular trends in obesity, regional adiposity and metabolic parameters among Asian Indian adolescents in north India: a comparative data analysis of two selective samples 5 years apart (2003, 2008). *Ann Nutr Metab*. 2010;56:176-81.
234. Wang Y, Chen H, Shaikh S, Mathur P. Is obesity becoming a public health problem in India? Examine the shift from under- to overnutrition problems over time. *Obesity Reviews*. 2009;10(4).
235. Ji C, Cheng TY. Epidemic increase in overweight and obesity in Chinese children from 1985 to 2005. *Int J Cardiol*. 2009(132):1-10.
236. Rassamee S, Ladda M-s, Virasakdi C, Chaon J. Secular increases in weight, height and body mass index among school children of Hat Yai, Thailand: a 5 years follow up study. *Southeast Asian J Trop Med Public Health*. 1999;30(3):532-8.
237. Hop L, Gross R, Giay T, Schultink W, Thuan B, Sastroamidjojo S. Longitudinal observation of growth of Vietnamese children in Hanoi, Vietnam from birth to 10 years of age. *European Journal of Clinical Nutrition*. 1997;51:164-71.
238. Wang Y, Lobstein T. Worldwide trends in childhood overweight and obesity. *International journal of pediatric obesity*. 2006;1 (1):11-25.
239. WHO. Physical status: the use and interpretation of anthropometry. Geneva: World Health Organization, 1995.
240. Low SM, Chin M, Ma S, Heng D, Deurenberg-Yap M. Rationale for redefining obesity in Asians. *Ann Acad Med Singapore*. 2009;38:66-9.
241. Misra A, Khurana L. Obesity-related non-communicable diseases: South Asians vs White Caucasians. *Int J Obes*. 2011;35:167-87.
242. Deurenberg-Yap M, Deurenberg P. Is a re-evaluation of WHO body mass index cut-off values needed? The case of Asians in Singapore. *Nutrition Reviews*. 2003;61(5):S80-S7.
243. Deurenberg-Yap M, Chew SK, Deurenberg P. Elevated body fat percentage and cardiovascular risks at low body mass index levels among Singaporean Chinese, Malays and Indians. *Obesity Reviews*. 2002;3:209-15.
244. de Wilde J, Van Dommelen P, Middelkoop B. Appropriate Body Mass Index Cut-Offs to determine thinness, overweight and obesity in South Asian children in The Netherlands. *PLoS ONE*. 2013;8(12):e82822.

245. WHO. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet*. 2004;363:157-63.
246. Bundred P, Kitchiner D, Buchan I. Prevalence of overweight and obese children between 1989 and 1998: population based series of cross sectional studies. *BMJ*. 2001;322:1-4.
247. Gorber S, Tremblay M, Moher D, Gorber B. A comparison of direct vs. self-report measures for assessing height, weight and body mass index: a systematic review. *Obesity Reviews*. 2007;8:307-26.
248. De Onis M. Measuring nutritional status in relation to mortality. *Bulletin of the World Health Organization*. 2000;78(10):1271-4.
249. Ho T, Chay S, Yip W, Tay J, Wong H. The prevalence of obesity in singapore primary school children. *Aust Paediatr J*. 1983;19(4):248-50.
250. Ploubidis G, Benova L, Grundy E, Laydon D, De Stavola B. Lifelong Socio Economic Position and biomarkers of later life health: Testing the contribution of competing hypotheses. *Social Science & Medicine*. 2014:1-8.
251. Silverwood R, Pierce M, Hardy R, Thomas C, Ferro C, Savage C, et al. Early-Life Overweight Trajectory and CKD in the 1946 British Birth Cohort Study. *Am J Kidney Dis*. 2013;62(2):276-84.
252. Ziol-Guest KM, Duncan G, Kalil A. Early Childhood Poverty and Adult Body Mass Index. *Am J Public Health*. 2009;99(3):527-32.
253. Wells NM, Evans G, Beavis A, Ong AD. Early childhood poverty, cumulative risk exposure, and body mass index trajectories through young adulthood. *Am J Public Health*. 2010;100(2):2507-12.
254. Kendzor DE, Caughy M, Owen MT. Family income trajectory during childhood is associated with adiposity in adolescence: a latent class growth analysis. *BMC Public Health*. 2012;12(611):611.
255. Pollitt RA, Rose KM, Kaufman J. Evaluating the evidence for models of life course socioeconomic factors and cardiovascular outcomes: a systematic review. *BMC Public Health*. 2005;5(7).
256. Williams A, Wyatt K, Hurst AJ, Anthony C. A systematic review of associations between the primary school built environment and childhood overweight and obesity. *Health & Place*. 2012;18(3):504-14.
257. Swinburn B, Egger G, Raza F. Dissecting obesogenic environments: the development and application of a framework for identifying and prioritizing environmental interventions for obesity. *Prev Med*. 1999;29(6):563-70.

258. Andruff H, Carraro N, Thompson A, Gaudreau P. Latent Class Growth Modelling: a tutorial. *Tutorials in Quantitative Methods for Psychology*. 2009;5(1):11-24.
259. Nylund K, Asparouhov T, Muthen BO. Deciding on the Number of Classes in Latent Class Analysis and Growth Mixture Modeling: A Monte Carlo Simulation Study. *Structural Equation Modeling*. 2007;14(4):535-69.
260. Pryor L, Tremblay R, Boivin M, Touchette E, Dubois L, Genolini C, et al. Developmental Trajectories of Body Mass Index in Early Childhood and Their Risk Factors. *Arch Pediatr Adolesc Med*. 2011;165(10):906-12.
261. Rzehak P, Wijga AH, Keil T, Eller E, Bindslev-Jensen C, Smit HA, et al. Body mass index trajectory classes and incident asthma in childhood: Results from 8 European Birth Cohorts—a Global Allergy and Asthma European Network initiative. *J Allergy Clin Immunol*. 2013;131(6):1528-36.
262. Warrington NM, Howe LD, Wu Y-y, Timpson N, Tilling K, Pennell CE, et al. Association of a Body Mass Index Genetic Risk Score with Growth throughout Childhood and Adolescence. *PLoS ONE*. 2013;8(11).
263. Sovio U, Timpson N, Warrington NM, Briollais L, Mook-Kanamori D. Association Between FTO Polymorphism, Adiposity Peak and Adiposity Rebound in The Northern Finland Birth Cohort 1966. *Atherosclerosis*. 2009;207:e42e5.
264. Dvornyk V, Waqar H. Genetics of age at menarche: a systematic review. *Hum Reprod*. 2012;18.
265. Wen X, Kleinman G, Gillman M, Rifas-Shiman S, Taveras EM. Childhood body mass index trajectories: modeling, characterizing, pairwise correlations and socio-demographic predictors of trajectory characteristics. *BMC Med Res Methodol*. 2012;12(38).
266. Ambrosini GL. Childhood dietary patterns and later obesity: a review of the evidence. *Proceedings of the Nutrition Society*. 2014;73:137-46.
267. Brown T, Summerbell C. Systematic review of school-based interventions that focus on changing dietary intake and physical activity levels to prevent childhood obesity: an update to the obesity guidance produced by the National Institute for Health and Clinical Excellence. *Obesity Reviews*. 2009;10:110-41.
268. Taryn M. Trajectories of growth in body mass index across childhood: Associations with maternal and paternal employment. *Social Science & Medicine*. 2012:1-9.
269. Jaime PC, Lock K. Do school based food and nutrition policies improve diet and reduce obesity? *Preventive Medicine*. 2009;48:45-53.

270. Schafer J, Graham J. Missing data: our view of the state of the art. *Psychological Methods*. 2002;7(2):147-77.
271. Shaw R, Green MJ, Popham F, Benzeval M. Differences in adiposity trajectories by birth cohort and childhood social class: evidence from cohorts born in the 1930s, 1950s and 1970s in the west of Scotland. *J Epidemiol Community Health*. 2014;1-7.
272. Mary S, Margaret M, Katheleen H, Barry L. Growth Trajectories of Preterm Infants: Birth to 12 Years. *Journal of Pediatric Health Care*. 2008;22:83-93.
273. Luppino FS, De Wit LM, Bouvy PF, Stijnen T, Cuijpers P, Penninx BW, et al. Overweight, Obesity, and Depression: a systematic review and meta-analysis of longitudinal studies. *Arch Gen Psychiatry*. 2010;67(3):220-9.
274. Subramaniam M, Picco L, He V, Vaingankar J, Abdin E, Verma S, et al. Body mass index and risk of mental disorders in the general population: Results from the Singapore Mental Health Study. *Journal of Psychosomatic Research*. 2013;74:135-41.
275. Zhang J, Yan F, Li Y, McKeown R. Body mass index and suicidal behaviors: A critical review of epidemiological evidence. *Journal of Affective Disorders*. 148;148:147-60.
276. Ferrari A, Norman R, Freedman G, Baxter A, Pirkis J, Harris M, et al. The burden attributable to mental and substance use disorders as risk factors for suicide: findings from the global burden of disease study 2010. *PLoS ONE*. 2014;9(4):e91936.
277. Vos T. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet*. 2012;15(380):2163-96.
278. Whiteford H, Degenhardt L, Rehm J, Baxter A, Ferrari A, Erskine H, et al. Global burden of disease attributable to mental and substance use disorders: findings from the Global Burden of Disease Study 2010. *Lancet*. 2013;382(9904):1575-86.
279. Kessler R. The Costs of Depression. *Psychiatr Clin North Am*. 2012;35(1):1-14.
280. Van der kooy K, Van hout H, Marwijk H, Marten H, Stehouwer CD, Beekman ATF. Depression and the risk for cardiovascular diseases: systematic review and meta analysis. *International Journal of Geriatric Psychiatry*. 2007;22:613-26.
281. Atlantis E, Baker M. Obesity effects on depression: systematic review of epidemiological studies. *International Journal of Obesity*. 2008;32:881-91.
282. De Wit LM, Luppino FS, Penninx BW, Zitman FG, Cuijpers P. Depression and obesity: a meta-analysis of community-based studies. *Psychiatry Res*. 2010;178(2):230-5.

283. Xu Q, Anderson D, Lurie-Beck J. The relationship between abdominal obesity and depression in the general population: A systematic review and meta-analysis. *Obesity Research & Clinical Practice*. 2011;5:e267-78.
284. Herva A, Laitinen J, Miettunen J, Veijola J, Karvonen J, Laksy K, et al. Obesity and depression: results from the longitudinal Northern Finland 1966 Birth Cohort Study. *International Journal of Obesity*. 2006;30:520-7.
285. Richardson LP, Davis R, Poulton R, McCauley E, Moffitt TE, Caspi A, et al. A longitudinal evaluation of adolescent depression and adult obesity. *Arch Pediatr Adolesc Med*. 2003;157(8):739-45.
286. Scott K, Bruffaerts R, Simon G, Alonso J, Angermeyer M, de Girolamo G. Obesity and mental disorders in the general population: results from the world mental health surveys. *Int J Obes*. 2007;32:192-200.
287. Incledon E, Wake M, Hay M. Psychological predictors of adiposity: systematic review of longitudinal studies. *Int J Pediatr Obes*. 2011;6(2-2):e1-11.
288. Korczak D, Lipman E, Morrison K, Szatmari P. Are children and adolescents with psychiatric illness at risk for increased future body weight? A systematic review. *Dev Med Child Neurol*. 2013;55(11):980-7.
289. Alberga A, Sigal RJ, Goldfield G, Prud Homme D, Kenny G. Overweight and obese teenagers: why is adolescence a critical period? *Pediatr Obes*. 2012;7(4):261-73.
290. Jacob K, Sharan P, Mirza I, Garrido-Cumbrera M, Seedat S, Mari J, et al. Mental health systems in countries: where are we now? *Lancet*. 2007;370:1061-77.
291. Fones C, Kua E, Ng T, Ko S. Studying the mental health of a nation; a preliminary report of a population survey in Singapore. *Singapore Med J*. 1998;39:251-5.
292. Chua H, Lim L, Ng T, Lee T, Mahendran R, Fones C. The prevalence of psychiatric disorders in Singapore adults. *Ann Acad Med Singapore*. 2004;33:S102.
293. Subramaniam M, Vaingankar J, Heng D, Kwok KW, Lim Y, Yap M, et al. The Singapore Mental Health Study: an overview of the methodology. *Int J Methods Psychiatr Res*. 2012;21(2):149-57.
294. Chong SA, Vaingankar J, Abidin E, Subramaniam M. The prevalence and impact of major depressive disorder among Chinese, Malays and Indians in an Asian multi-racial population. *Journal of Affective Disorders*. 2012;138:128-36.
295. Kessler RC, Birnbaum H, Shahly V, Bromet E, Hwang I, McLaughlin K, et al. Age differences in the prevalence and co-morbidity of DSM-IV major depressive episodes: results from the WHO World Mental Health Survey Initiative. *Depress Anxiety*. 2010;27(4):351-64.

296. Huang D, Lanza H, Wright-volel K, Anglin M. Developmental trajectories of childhood obesity and risk behaviors in adolescence. *Journal of Adolescence*. 2013;36:139-48.
297. Goldberg D, Hillier V. A scaled version of the General Health Questionnaire. *Psychol Med*. 1979;9:139-45.
298. Tait R, Hulse G, Robertson S. A review of the validity of the General Health Questionnaire in adolescent populations. *Aust N Z J Psychiatry*. 2002;36(4):550-7.
299. Shevlin M, Adamson G. Alternative Factor Models and Factorial Invariance of the GHQ-12: A Large Sample Analysis Using Confirmatory Factor Analysis. *Psychological Assessment*. 2005(17):231-6.
300. Graetz B. Multidimensional properties of the General Health Questionnaire. *Social Psychiatry and Psychiatric Epidemiology*. 1991;26(3):132-8.
301. Hankins M. The reliability of the twelve-item general health questionnaire (GHQ-12) under realistic assumptions. *BMC Public Health*. 2008;8:355.
302. Mood C. Logistic regression: why we cannot do what we think we can do, and what we can do about it. *European Sociological Review*. 2010;26(1):67-82.
303. Pallan MJ, Adab P, Sitch A, Aveyard P. Are school physical activity characteristics associated with weight status in primary school children? A multilevel cross-sectional analysis of routine surveillance data. *Arch Dis Child*. 2014;99:135-41.
304. Lissner L, Sohlstrom A, Sundblom E, Sjoberg A. Trends in overweight and obesity in Swedish schoolchildren 1999-2005: has the epidemic reached a plateau? *Obes Rev*. 2010;11(8):553-9.
305. Petersen T, Rasmussen S, Madsen M. BMI of Danish school children measured during the periods 1986/1987--1996/1997 compared to Danish measurement in 1971/1972. *Ugeskr Laeger*. 2002;164(43):5006-10.
306. Northstone K, Guggenheim J, Howe L, Tilling K, Paternoster L, Kemp J, et al. Body stature growth trajectories during childhood and the development of myopia. *Ophthalmology*. 2013(In Press).
307. Herva A, Laitinen J, Miettunen J, Veijola J, Karvonen JT, Lakso K, et al. Obesity and depression: results from the longitudinal Northern Finland 1966 Birth Cohort Study. *International Journal of Obesity*. 2006;30(3):520-7.
308. Anderson S, Cohen P, Naumova E, Jacques PF, Must A. Adolescent obesity and risk for subsequent major depressive disorder and anxiety disorder: prospective evidence. *Psychosom Med*. 2007;69(8):740-7.



309. Lucassen E, Cizza G. The Hypothalamic-Pituitary-Adrenal Axis, Obesity, and Chronic Stress Exposure: Sleep and the HPA Axis in Obesity. *Curr Obes Rep.* 2012;1(4):208-15.
310. Yehuda R, Teicher M, Trestman R, Levengood R, Siever L. Cortisol regulation in posttraumatic stress disorder and major depression: a chronobiological analysis. *Bio Psychiatry.* 1996;40(2):79-88.
311. Faravelli C, Lo Sauro C, Lelli L, Pietrini F, Lazzeretti L, Godini L, et al. Childhood stressful events, HPA axis and anxiety disorders. *Curr Pharm Des.* 2012;18(35):5663-74.
312. Xie B, Liu C, Chou C, Xia J, Spruijt-Metz D, Gong J, et al. Weight perception and psychological factors in Chinese adolescents. *J Adolesc Health.* 2003;33(3):202-10.
313. Stankov I, Olds T, Cargo M. Overweight and obese adolescents: what turns them off physical activity? *International journal of behavioral nutrition and Physical Activity.* 2012;9(53).
314. Power C, Thomas C. Changes in BMI, duration of overweight and obesity, and glucose metabolism: 45 years of follow-up of a birth cohort. *Diabetes Care.* 2011;34(9):1986-91.
315. Everhart JE, Pettitt DJ, Bennett P. Duration of obesity increases the incidence of NIDDM. *Diabetes.* 1992(41):235-40.
316. Wannamethee S, Shaper A. Weight change and duration of overweight and obesity. *Diabetes Care.* 1999(22):1266-72.
317. Lopresti A, Drummond P. Obesity and psychiatric disorders: Commonalities in dysregulated biological pathways and their implications for treatment. *Progress in Neuro Psychopharmacology & Biological Psychiatry.* 2013;45:92-9.
318. Maes M, Kubera M, Obuchowiczwa E, Goehler L, Brzeszcz J. Depression's multiple comorbidities explained by (neuro)inflammatory and oxidative & nitrosative. *Neuro Endocrinol Lett.* 2011;32(1):7-24.
319. Yap BH, Pilkington P, Ryan S. Parental factors associated with depression and anxiety in young people: a systematic review and meta-analysis. *Journal of Affective Disorders.* 2014;156:8-23.
320. Lopresti A, Hood S, Drummond P. A review of lifestyle factors that contribute to important pathways associated with major depression: Diet, sleep and exercise. *Journal of Affective Disorders.* 2013;148:12-27.
321. Yang S, Tilling K, Martin R, Davies N, Ben-Shlomo Y, Kramer MS. Pre-natal and post-natal growth trajectories and childhood cognitive ability and mental health. *International Journal of Epidemiology.* 2011;40:1215-226.

322. Alford A. The association of fetal and early childhood growth with adult mental distress: evidence from the Johns Hopkins Collaborative Perinatal Study birth cohort. *Frontiers in Psychiatry*. 2013;4:96.
323. De Onis M. The use of anthropometry in the prevention of childhood overweight and obesity. *International Journal of Obesity*. 2004;28:S81-5.
324. Mason J, Mitchell J. Nutritional surveillance. *Bull World Health Organ*. 1983;61(5):745-55.
325. Ho T, Yip W, Tay J, Rajan U. Social class distribution of obese Chinese children. *J Singapore Paediatr Soc*. 1991;33(1):55-8.
326. Ryder N. The cohort as a concept in the study of social change. *American Sociological Review*. 1965;30(6):843-61.
327. Araujo de Franca G, Restrepo-mendez M, Loret de Mola C, Victora CG. Size at birth and abdominal adiposity in adults: a systematic review and meta-analysis. *Obes Rev*. 2014;15(2):77-91.
328. Baird J, Fisher D, Lucas P, Kleijnen J, Roberts H, Law C. Being big or growing fast: systematic review of size and growth in infancy and later obesity. *British Medical Journal*. 2005;331:929.
329. Karlberg J. On the construction of the infancy-childhood-puberty growth standard. *Acta Paediatr Scand*. 1989;356:26-37.
330. Liu Y, Albertsson Wikland K, Karlberg J. New reference for the age at childhood onset of growth and secular trend in the timing of puberty in Swedish. *Acta Paediatr*. 2000;89:637-43.
331. Tse W, Hindmarsh PC, Brook CG. The infancy-childhood-puberty model of growth: clinical aspects. *Acta Paediatr Scand*. 1989;356:38-43.
332. Xu X, Wang W, Guo Z, Karlberg J. Longitudinal Growth During Infancy and Childhood in Children from Shanghai: Predictors and Consequences of the Age at Onset of the Childhood Phase of Growth. *Pediatric Research*. 2002;51(3):377-85.
333. Ji C, Cheng T. Epidemic increase in overweight and obesity in Chinese children from 1985 to 2005. *Int J Cardiol*. 2009;132:1-10.
334. Dieu H, Dibley M, Sibbritt D, Hanh T. Trends in overweight and obesity in pre-school children in urban areas of Ho Chi Minh City, Vietnam, from 2002 to 2005. *Public Health Nutr*. 2009;12:702-9.
335. Doak CM, Adair L, Monteiro C, Popkin B. Overweight and underweight coexist within households in Brazil, China and Russia. *Journal of Nutrition*. 2000;130(12):2965-71.

336. Dearth-Wesley T, Wang H, Popkin B. Under- and overnutrition dynamics in Chinese children and adults (1991-2004). *European Journal of Clinical Nutrition*. 2008;62:1302-7.
337. Wang Y, Beydoun MA, Li J, Liu Y, Moreno L. Do children and their parents eat a similar diet? Resemblance in child and parental dietary intake--systematic review and metaanalysis. *J Epidemiol Community Health*. 2011;65(2):177-89.
338. Poh B, Kathryn TB, Wong S, Chee S, Tee E. Nutritional status, dietary intake patterns and nutrition knowledge of children aged 5-6 years attending kindergartens in the Klang Valley, Malaysia. *Malaysian Journal of Nutrition*. 2012;18(2):231-42.
339. Yung T, Lee A, Ho M, Keung V, Lee J. Maternal influences on fruit and vegetable consumption of schoolchildren: case study in Hong Kong. *Matern Child Nutr*. 2010;6(2):190-8.
340. Kremers S, Sleddens E, Gerald S, Gubbels J, Rodenburg G, Gevers D, et al. General and food-specific parenting: measures and interplay. *Child Obes*. 2013;9(Supplement 1):S22-31.
341. MOH. National Nutrition Survey 1993. Singapore: Department of Nutrition, Ministry of Health, 1993.
342. MOH. National Nutrition Survey 1998. Singapore: Department of Nutrition, Ministry of Health, 1998.
343. HPB. National Nutrition Survey 2004. Singapore: Health Promotion Board, 2004.
344. HPB. National Nutrition Survey 2010. Singapore: Health Promotion Board, 2010.
345. Yu-Kang T, Tilling K, Sterne JAC, Gilthorpe M. A critical evaluation of statistical approaches to examining the role of growth trajectories in the developmental origins of health and disease. *International Journal of Epidemiology*. 2013;42:1327-39.
346. Power C, Lake JK, Cole T. Measurement and long-term health risks of child and adolescent fatness. *Int J Obes Relat Metab Disord*. 1997;21(7):507-26.
347. Must A, Jacques PF, Dallal GE, Bajema C, Dietz W. Long-term morbidity and mortality of overweight adolescents. A follow-up of the Harvard Growth Study of 1922 to 1935. *N Engl J Med*. 1992;327(19):1350-5.
348. Lloyd LJ, Langley-Evans SC, McMullen S. Childhood obesity and risk of the adult metabolic syndrome: a systematic review. *International Journal of Obesity*. 2012;36:1-11.
349. Cordoba-Chacon J, Gahete M, Pozo-Salas A, Moreno-Herrera A, Castano J, Kineman R, et al. Peripubertal-onset but not adult-onset obesity increases IGF-I and drives development of lean mass, which may lessen the metabolic impairment in adult obesity. *Am J Physiol Endocrinol Metab*. 2012;303:E1151-7.

350. Kanbur NO, Derman O, Kinik E. Prevalence of obesity in adolescents and the impact of sexual maturation stage on body mass index in obese adolescents. *Int J Adolesc Med Health*. 2002;14(1):61-5.
351. Cheng G, Buyken AE, Shi L, Karaolis-Danckert N, Kroke A, Wudy S, et al. Beyond overweight: nutrition as an important lifestyle factor influencing timing of puberty. *Nutrition Reviews*. 2012;70(3):133-52.
352. HPB. HPB launches new mental health initiatives to help youth bounce back stronger from life's challenges Singapore: HPB; 2012 [cited 2014 21st May]. Available from: [http://www.hpb.gov.sg/HOPPortal/content/conn/HOPUCM/path/Contribution%20Folders/HPB%20Online/News%20and%20Events/News/2012///Media%20Release\\_Bounce%20Back%20Stronger\\_FINAL%20\(website\).pdf](http://www.hpb.gov.sg/HOPPortal/content/conn/HOPUCM/path/Contribution%20Folders/HPB%20Online/News%20and%20Events/News/2012///Media%20Release_Bounce%20Back%20Stronger_FINAL%20(website).pdf).
353. HPB. Mental Wellness Singapore: HPB; 2011 [cited 2014 21st May]. Available from: [breathe.sg](http://breathe.sg).
354. Calear A, Christensen H. Review of internet-based prevention and treatment programs for anxiety and depression in children and adolescents. *Med J Aust*. 2010;192(Suppl 11):S12-4.
355. Cali AM, Caprio S. Obesity in Children and Adolescents. *J Clin Endocrinol Metab*. 2008;93(Suppl 1):S31-S6.
356. Solorzano CB, McCartney CR. Obesity and the pubertal transition in girls and boys. *Reproduction*. 2010;140(3):399-410.
357. Prentice P, Viner R. Pubertal timing and adult obesity and cardiometabolic risk in women and men: a systematic review and meta-analysis. *International Journal of Obesity*. 2013;37:1036-43.
358. Kim J, So WY. Association between overweight/obesity and academic performance in South Korean adolescents. *Cent Eur J Public Health*. 2013;21(4):179-83.
359. Kaestner R, Grossman M. Effects of weight on children's education achievement. Cambridge, MA: National Bureau of Economics Research, 2008.
360. Siraj-Blatchford I, Mayo A, Melhuish E, Taggart B, Sammons P, Sylva K. Performing against the odds: developmental trajectories of children in the EPPSE 3-16 study. London: Department of Education, UK Government, 2011.
361. Crosnoe R, Muller C. Body Mass Index, Academic Achievement, and School Context: Examining the Educational Experiences of Adolescents at Risk of Obesity. *Journal of Health and Social Behavior*. 2004;45(4):393-407.

362. Henry K. Academic Achievement and Adolescent Drug Use: An Examination of Reciprocal Effects and Correlated Growth Trajectories. *Journal of School Health*. 2010;80(1):38-43.
363. Singstats. General Household Survey 2005. Singapore: Singstats, 2005.
364. Bauer K, Hearst MO, Escoto K, Berge J, Neumark-Sztainer D. Parental employment and work-family stress: associations with family food environments. *Soc Sci Med*. 2012;75(3):496-504.
365. Anderson P, Butcher K. Childhood obesity: trends and potential causes. *Future Child*. 2006;16(1):19-45.
366. Morrissey T. Trajectories of growth in body mass index across childhood: Associations with maternal and paternal employment. *Social Science & Medicine*. 2013;95:60-8.
367. Leslie C. Walkability of local communities: Using geographic information systems to objectively assess relevant environmental attributes. *Health & Place*. 2007;13(1):111-22.
368. McGinn. Exploring associations between physical activity and perceived and objective measures of the built environment. *Journal of Urban Health*. 2007;84(2):162-84.
369. Pikora T. Developing a reliable audit instrument to measure the physical environment for physical activity. *American Journal of Preventive Medicine*. 2002;23(3):187-94.
370. Jago R. Observed, GIS, and self-reported environmental features and adolescent physical activity. *American Journal of Health Promotion*. 2006;20(6):422-8.
371. Owen N. Neighborhood walkability and the walking behavior of Australian adults. *American Journal of Preventive Medicine*. 2007;33:387-95.
372. MOF. Data.gov.sg Singapore2011 [cited 2014 21st May]. Available from: <http://www.data.gov.sg/>.
373. Yu Zb et al. Birth weight and subsequent risk of obesity: a systematic review and meta-analysis. *Obesity Review*. 2011;12(7):525-42.
374. Taylor et al. Early adiposity rebound: review of papers linking this to subsequent obesity in children and adults. *Curr Opin Clin Nutr Metab Care*. 2005;8(6):607-12.